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CHOLERA.

RUSSELL (A. J. H.). **Cholera in India.**—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 389–398.

CHUN (J. W. H.). **An Analysis of the Cholera Problem in China with Special Reference to Shanghai.**—*Ibid.* pp. 399–409.

POLLITZER (R.). **The Behaviour of Cholera and Cholera-like Vibrios towards Blood and Milk Media.**—*Ibid.* pp. 411–419.

YANG (Y. N.). **A Serological Study on Cholera Vibrios.**—*Ibid.* pp. 421–429.

FAR EASTERN ASSOCIATION OF TROPICAL MEDICINE. TRANSACTIONS NINTH CONGRESS, NANKING, CHINA, 1934. Vol. 1. pp. 431–450. —**Round Table Discussion on Cholera** [RUSSELL (A. J. H.), Chairman.]

A representative international conference on cholera attended by men with experience of the disease and held in one of the countries which is periodically afflicted with outbreaks of the disease has international importance. All the present controversial matter received its share of attention and ranged over such subjects as epidemiology, prophylaxis, classification, the vaccine and bacteriophage. Only some of the points dealt with can be commented upon and especially those of the nature of conclusions or proposals. These seem to have been restrained, critical and cautious, and their tenor to have been the necessity for a fresh examination of the whole subject of cholera and the cholera vibrio on a controlled and statistical basis.

Epidemiology and Prophylaxis.—Of the climatic factors which might be considered as related to cholera rainfall was picked out for special notice. Rainfall was not accepted by Russell as having any direct effect on incidence. It merely distributes infection. Epidemic areas have a combination of high relative humidity and high temperature, while these are not essential in an endemic area. The endemic areas [or as we may call them the homes of cholera] are the great rivers of the East and especially their deltaic tracts. In India the decennium 1923–32 shows the lowest incidence of cholera on record and in seeking for causes for this result Russell makes mention of two possible factors, the extension of public health service and the distribution of bacteriophage, with the qualifying remark: "Future experience . . . will prove . . . whether these new factors have had the effect which enthusiasts may be inclined to claim on their behalf."

He abandons the tentative attitude implied in this statement, however, when he says of anti-cholera vaccine. "The statistics we

possess . . . prove conclusively that in this prophylactic . . . we have a valuable preventive weapon against cholera." It is also evident that he is an advocate, on statistical grounds, of the greater efficacy of bilivaccine *per os* over subcutaneous anti-cholera vaccine, and it is surprising to find that the "Office International" when referred to on this point "declared that while vaccination *per os* probably produces a certain immunity, this is much inferior to that obtained by subcutaneous inoculation." Other contributors to the subject of the epidemiology of cholera dealt to some extent with endemicity. Thus Chun says with some emphasis, "To our mind there is little doubt that cholera is endemic in the central Yangtze valley" and "The more we study the cholera problem the less tenable becomes the theory of an importation of the infection." [Such pronouncements should go some way towards dispelling the notion that Bengal is *the* home of cholera.]

Vibrio Classification.—Russell referred to the investigation of 4,000 vibrios freshly isolated in Calcutta from cholera cases, convalescents, carriers and from nature. "The main conclusion reached is that there is a very close relationship between the so-called 'authentic cholera vibrio' and the other vibrios." In the work of Pollitzer a further vibrio character—the curdling of milk—was added to those of haemodigestion and haemolysis for the purpose of grouping. He seems inclined to admit the possible existence of strains intermediate in character "between the ordinary water vibrios (which they resembled in blood and milk reactions) and the typical cholera vibrios (to which they belonged serologically)." Yang considered the subject of transformation and claims to have effected the transformation of non-agglutinable water vibrios into agglutinable vibrios by "daily transfers in sheep serum broth or broth."

Bacteriophage.—A communication by PANDIT dealt with the use of bacteriophage. His verdict may be very briefly expressed as follows: In treatment the evidence was that, administered within the first 24 hours of the disease a 50 per cent. reduction of mortality might be expected but that after 23 hours there was no reduction. The case for prophylactic value was stated as: (*a*) that it did not prevent the onset of infection but had an effect similar to that of administration curatively within 24 hours of the disease; and (*b*) that it reduced the number of secondary cases in a treated area.

Vaccine.—Russell who, as already stated, is in favour of the use of anti-cholera vaccine prophylactically also alludes to the different action of the particulate and fluid components of a vaccine. "The immunising value of cholera vaccines prepared (*a*) from bacterial deposit, (*b*) from the supernatant fluid, and (*c*) from a mixture of deposit and supernatant fluid has revealed that vaccines prepared from supernatant fluid are not only very toxic but possess little protective value. Those prepared from bacterial deposit are highly protective." [The reverse would appear to hold good of plague vaccine.]

Discussion.—In the round table discussion following the papers many delegates took part. The trend of the discussion is embodied in certain general resolutions. They were that: 1. Further investigation is desirable into the question of "carriers" of cholera and this should be carried out in the countries of the Far East. 2. Further statistically controlled field tests should be carried out of the protection conferred by anti-cholera vaccine especially in those countries where such tests have not yet been done. 3. Further study of the relationship

between the cholera vibrios and their variants is desirable. 4. Further field and statistical work should be carried out to obtain more exact information regarding the epidemic and endemic areas for cholera in the Far East. *W. F. Harvey.*

NICHOLLS (Lucius). **Carriers of *V. cholerae* who enter Ceylon from South India.**—*Indian Jl. Med. Res.* 1935. Apr. Vol. 22. No. 4. pp. 713–744. With 2 maps & 3 graphs.

Much information regarding carriage of the cholera vibrio, the infectivity of the carrier, and the relation of non-agglutinable cholera-like vibrios to the true cholera vibrio may be derived from quarantine camps such as the well-known camp of Tor and that which is here in question at Mandapam in South India, especially if the data are taken in conjunction with developments after departure from quarantine. At Mandapam camp the stools of as many labourers and 3rd class passengers as possible are examined for *V. cholerae* and even though an agglutinable vibrio is found this does not mean any delay in continuation of the journey to Ceylon. All the vibrios isolated are placed in three groups which are compared with the cholera vibrio: I agglutinable, cholera-like; II non-agglutinable but cholera-like; and III non-agglutinable, morphologically and culturally unlike, vibrios. Samples of stools from 100,896 persons have been examined. Group I vibrios were isolated 84 times, Group II 2,838 times and Group III 992 times. We turn now to the records of cholera in Ceylon for 9 years 1925 to 1933. "Cholera has occurred on 30 occasions in the 9 years under consideration. On 21 occasions only one person was affected and the other 9 were outbreaks in which 3 or more persons acquired cholera." This is not a serious epidemiological history. On 10 occasions cholera occurred in the areas to which the estate labourers went and "on 9 of these occasions the disease was due to a recent arrival being in the incubation period." The nature of the journey to Ceylon was such as should have facilitated distribution of the cholera vibrio and therefore: "Since no case of cholera has occurred in Ceylon for the last ten years, in which it could be assumed that the patient had acquired the infection on the journey, it is strong evidence for the low virulence of the agglutinating vibrios of carriers." Nevertheless the author does not subscribe wholly to the view that only persons actually suffering from cholera and those in the incubation stage are infective. As regards seasonal prevalence and the relation of cholera-like to the cholera vibrios, it was found that during the cholera season in Madras Group II vibrios may occur in 10 per cent. of the estate labourers and that the prevalence of this group falls to 1 or 2 per cent. during the dry season. By "taking all the evidence into consideration it is difficult to avoid the conclusion that the vibrios of Group II are non-agglutinable avirulent *V. cholerae.*" [See also *Trop. Dis. Bull.* 1934. Vol. 31. Suppl. p. 112*.] *W. F. H.*

DOORENBOS (W.). Note préliminaire sur la recherche des porteurs de vibrions au lazaret de Tor, chez les pèlerins retournant du Hedjaz. [**Vibrio Carriers at Tor in Pilgrims from the Hejaz.**]—*Bull. Office Internat. d'Hyg. Publique.* 1935. Feb. Vol. 27. No. 2. pp. 268–272. With 1 fig.

The total number of examinations for vibrio carriers made at Tor since 1930 is 39,217. All the vibrios isolated have been minutely

examined in the laboratories of Tor and Alexandria, and their agglutinability tested with various sera including a " standard " serum. It is obvious that the experience accumulated on such a large body of evidence must be of the greatest importance in connexion with the identification of the true cholera vibrio and the value of the measures adopted for control of spread of the disease. Agglutinating and non-agglutinating vibrios have been found at Tor but during the last five annual pilgrimages not a case of cholera has declared itself at this encampment.

The author enunciates his well-known views in this article, views which would gather within the fold of the true cholera vibrio the El Tor vibrio, paracholera vibrios, and others under the denomination of endemic disequilibrated cholera vibrios of low virulence, causative only of sporadic cholera. The epidemic form of cholera is due to a contrasted type, the *Vibrio cholerae typus epidemicus* (see this *Bulletin, ante*, p. 457). *W. F. H.*

BANERJEE (Dhirendra Nath) & DATTA (Sunil Krisna). **Cholera Kidney—a Histological Study.**—*Jl. Indian Med. Assoc.* 1935. June. Vol. 4. No. 10. pp. 441–444.

Twenty-six specimens of cholera kidney were examined and five of these were from patients dead of uraemia with total anuria for several days. A large range of special stains were used. The results were that: 1. With ordinary stains very little change could be detected in the glomeruli. 2. The glomeruli showed, with special staining, " thickening of the basement membrane with proliferation of both the epithelial and endothelial cells of the tuft." In many of the glomeruli focal necrosis, with hyaline change and sclerotic atrophy, was prominent. These were invariably present in all patients dying of uraemia. 3. Tubular changes were those of the epithelium of the convoluted tubules. Various casts were present in the tubules. 4. Interlobular vessels were always thickened in cases of uraemia.

W. F. H.

NARAYANA RAO (Y. S.). **A Plea for the Use of Concentrated Saline in Cholera.** [Correspondence.]—*Indian Med. Gaz.* 1935. May. Vol. 70. No. 5. pp. 296–297.

The question is asked by the author whether the advantage of administration of hypertonic salt solution in cholera may not lie more in the intravenous administration of salt than of the fluid in which it is dissolved. That this supposition has some foundation seemed to emerge from the treatment of four collapsed or collapsing cases of cholera with not more than 20 cc. of 20 per cent. salt solution and the revival of the circulation—as indicated by the passing of urine—within a few minutes after injection. At least the method might, on account of its simplicity, provide a first aid measure.

W. F. H.

MORISON (J.). **Bacteriophage in Cholera.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Apr. 17. Vol. 28. No. 6. pp. 563–570.

Although in this communication Morison traverses well-known ground there is always matter of interest in the most recent expression

of views on the nature and mode of action of bacteriophage. At the present time eleven types of cholera bacteriophage have been isolated. This is an addition of two new ones to the former nine. Nor are the types wanting in distinctness. They " are as distinct from each other as species."

Perhaps one of the most interesting phenomena in connexion with the phage question is that which relates to the resistance or susceptibility of suitable cholera vibrios to phage action. Its importance lies in the way in which it is used for the analysis of phage types. " If we use a strain of cholera vibrio lysable by all our phages and grow it in tubes of broth each containing one of the types of phage, we get strains of cholera, each of which is resistant to one type of phage and is lysable by all the other types. Again, if we grow a susceptible cholera vibrio with all but one of these types, it becomes resistant to all but one of the phages." A series of communications have been appearing now for some time on the extraordinary effect of phage in causing transformation of the characters of an organism. In this connexion what we may call Morison's " 511 experiment " is of great interest. " When cholera phage types were taken in combinations of two or more at a time the action of the combination was frequently different from the action of the individual components of the combination. This suggested an experiment in which the 511 possible combinations of our nine types of phage were tested on the same smooth *Vibrio cholerae*. The result was that we had changes in the morphology, the colonies on agar, the growth in broth, the salt stability, the agglutinability and the ability to ferment sugars which varied with the combination of types of bacteriophage and the period of action." These are remarkable changes especially if they are in any sense permanent and irreversible. Much of the main action of a phage, the solution of its corresponding bacterium, is ascribed to hydrolysis of the bacterial protein. Here also it is claimed that " no two types of phage exert the same enzyme action."

The second part of this informative article is occupied with the Nowgong-Habigunj field trials and it concludes with a reference to other bacteria awaiting the attentions of the worker with phages and phage types, " diseases like diphtheria, scarlet fever, streptococcal infections, coli infections, influenza and the typhoid group which show rises and falls in their virulence which have not yet been explained."

W. F. H.

WASSÉN (Anders). Essais d'application au vibrion cholérique de la méthode fondée sur la faculté de déplacement des bactéries. [**Attempts to apply to the Cholera Vibrio Methods founded on Differential Separation of Bacteria.**]—*Bull. Office Internat. d'Hyg. Publique.* 1935. June. Vol. 27. No. 6. pp. 1121–1134. With 2 figs. on 1 plate.

The methods referred to depend essentially on the motility of the organisms concerned and the use of filter paper saturated with an " H " specific agglutinating serum imbedded in a suitable semi-solid agar medium. Such a medium sown with artificially prepared test faecal material and incubated should give a differential outward movement of the specific bacteria, which will enable them to be collected and isolated for diagnosis. The method has proved, so far,

successful with paratyphoid organisms. In the case of the cholera vibrio very successful enrichment methods, using peptone water or alkaline blood are already known and employed. It remains to be seen what, in actual practice, this new technique can do. The medium used, containing usually 3 per cent. peptone (Parke Davis), 1 per cent. Liebig's extract, 0·3 per cent. sod. chloride and 0·35 per cent. agar, had a pH of 8·6. It is necessary to alkalinize it with sod. hydrate (1 cc. 10 per cent. per 100 cc. medium) and not sod. carbonate and to dilute it, if not of the right consistency, with 3 per cent. peptone bouillon. Other additions, intended to restrict the movement of organisms such as *Proteus vulgaris*, *Bact. coli* and *Ps. pyocyanea*, were: for 100 cc. medium 5 cc. 0·1 per cent. cadmium chloride and 5 cc. 1 per cent. pot. chlorate. The sod. hydrate and cadmium chloride must be mixed separately with the agar in order to avoid precipitation. An artificial stool containing, it might be, as few as 7 cholera vibrios, was introduced into the medium in amounts of 0·5 to 1 cc., at the side of the glass container by means of a pipette: care was taken to push the point of the pipette in various directions so as to lacerate the agar, and also to make the inoculation at a distance of a few millimetres from the wall. Strips of filter paper (5 × 20 mm.), saturated with specific serum (titre 1 : 25,000 and dilution 1 : 5), were inserted close to the inoculum and produced a characteristic agglutination of the advancing organisms, if these were specific. The appearances can be read off, after a variable time at 37°C., as positive or negative.

The author hopes that his method may result in the saving of an appreciable amount of time on the accredited methods for diagnosis of cholera. *W. F. H.*

PHAM (H. C.). L'action de l'endotoxine cholérique sur le système neuro-végétatif abdominal. [**The Action of Cholera Endotoxin on the Abdominal Sympathetic System.**]—*C. R. Soc. Biol.* 1935. Vol. 119. No. 16. pp. 78–80.

On the analogy of similar work with typho-paratyphoid endotoxin the author has injected small doses (0·05 to 0·1 cc.) of cholera endotoxin in the neighbourhood of the splanchnic nerve in guineapigs (460 gm.). The symptoms and lesions resembled those of cholera; similar results were obtained in the rabbit in doses of 0·2 cc. These symptoms were: dyspnoea, hypothermy, abdominal distension, and death in a few hours. With smaller doses the death of the animal was delayed for 3 or 4 days and it showed diarrhoea, oliguria, marked albuminuria and emaciation. Post-mortem there were found ecchymosis on the caecum, haemorrhagic infiltration of the terminal portion of the small intestine, congestion of Peyer's patches, desquamation of the mucosa the débris of which was found in the lumen of the intestine, vascular dilatation and haemorrhage, hyaline degeneration, oedema and haemorrhage in renal glomeruli, with some endothelial proliferation and cytolysis of tubular epithelium. Except for some diffuse parenchymatous hepatitis and suprarenal hyperaemia the other organs appeared normal. The doses used to produce these effects contrast markedly with the trivial effects produced by a subcutaneous injection of as much as 1 cc. endotoxin and with the lethal dose (about 0·8 cc.) by intra-cardiac injection. *W. F. H.*

TAKANO (Shichiro). **Studies concerning Immunological Variability of Cholera Vibrio.**—*Kitasato Arch. Experim. Med.* 1935. Apr. Vol. 12. No. 2. pp. 101–138. [27 refs.] [Summary appears also in *Bulletin of Hygiene.*]

A large amount of work has been carried out on the mutation or transformation of cholera vibrios and much controversy has arisen as to the identity of various vibrios found in nature with these artificially transmuted cholera organisms. Most of the author's investigation deals with the variations which can be produced by growing the cholera vibrio in immune sera. Two types of known vibrio immune sera were used, the Inaba or normal type and the Takano or atypical serum. The corresponding strains were each cultivated in bouillon containing one or other of the immune sera, that is each in a homologous and a heterologous serum respectively. By repeated cultivation in these media four variant strains were obtained, all of them highly motile, giving opaque colonies on agar, the surfaces of which were rough dry and granular, and all spontaneously agglutinable. In other cultural respects the four strains differed from one another. Serologically the four variant strains were divisible into three types: No. 1 type " was obtained by culturing typical strains in an immune serum of the typical strain," with the result that it became difficult of agglutination by the immune serum of either a typical or atypical strain. No. 2 type emerged by cultivation of an atypical strain in an atypical, that is homologous, serum by which it became a typical strain; and No. 3 type was " obtained by culturing a typical strain in immune serum of an atypical strain." This last type was unchanged by the cultivation. It was further found that the characters acquired by these strains did not change by cultivation in ordinary agar media for as many as 150 generations. *W. F. H.*

TAYLOR (J.) & AHUJA (M. L.). **Serological Relationships of Certain Vibrios isolated from Non-Cholera Sources in India.**—*Indian Jl. Med. Res.* 1935. July. Vol. 23. No. 1. pp. 95–119. With 10 charts. [Summary appears also in *Bulletin of Hygiene.*]

The characters of the true cholera vibrio seem to be as far off settlement as ever. In this publication a minute investigation is carried out into serological characters of (1) vibrios isolated from healthy individuals in an endemic area, (*a*) agglutinable and (*b*) inagglutinable, and (2) a vibrio isolated from water in a non-endemic area which had been free from epidemic cholera for a prolonged period. For the investigation high titre sera and suitable suspensions of test organisms which were intended to bring out " O " and " H " agglutination were used. The sera were prepared with (*a*) living vibrios, (*b*) suspensions heated at 55°C. for 30 minutes and suspensions boiled in alcohol for 1 hour respectively while the testing suspensions were (*a*) living cultures, (*b*) formalinized cultures, and (*c*) cultures heated at 100°C. for 1 hour.

The results are summarized as follows: (1) Agglutinable vibrios isolated from healthy individuals in an endemic cholera area have been found to be serologically indistinguishable from an authentic vibrio strain maintained in subculture. (2) A vibrio isolated from water in an area widely removed from places where cholera is endemic and which had been free from cholera for a number of years was

inagglutinable when first received, but in a period of 6-months' subculture developed all the biological characters of an authentic cholera vibrio including " H " and " O " agglutination to full titre, and was indistinguishable from a cholera strain when quantitative and qualitative tests were applied. This strain differed in chemical structure from the cholera strain with which it was compared and from the agglutinable " carrier " vibrios. (3) Vibrios possessing five different types of chemical structure, as shown by the nature of their protein and carbohydrate fractions, have given identical serological and biochemical reactions. (4) A series of inagglutinable vibrios isolated from healthy individuals in the same endemic cholera area have not been found to fall into any consistent serological group. *W. F. H.*

LINTON (Richard W.) ; MITRA (B. N.) ; SEAL (S. C.) ; SHRIVASTAVA (D. L.). **Studies on the Antigenic Structure of** *Vibrio cholerae.* **Part VIII. The Specific Carbohydrate Content and Serology of the Acid-Soluble Fractions** [LINTON, MITRA & SEAL].—*Indian Jl. Med. Res.* 1935. Apr. Vol. 22. No. 4. pp. 617–631. With 1 graph. **Part IX. Dissociation and Changes in Chemical Structure** [LINTON, SHRIVASTAVA & MITRA].—*Ibid.* pp. 633–657. With 3 figs. on 1 plate. [20 refs.]

Part VIII. A previous study [*ante*, p. 461] had reference to the three fractions " A," " B " and residue into which vibrios can be divided by extraction with acid alcohol. It has now been found that reducing substance (carbohydrate) " is present in both the fractions and in the residue and that the quantity in the latter is minute in proportion to the amount of the latter, which averages 85 per cent. of the whole vibrio. The ' A ' and ' B ' fractions have . . . proportionately large amounts of reducing substance." The " A " fraction probably represents the outer parts of the vibrio and shows high serological activity while " the ' B ' and residue portions are almost inactive, although capable of giving rise to active, non-specific anti-sera. The anti-serum to the ' A ' fraction is also non-specific." " A parallelism appears to exist between smoothness, as shown by . . . . . Millon's reagent, and the presence of more reducing substance in ' A ' than in ' B ' fraction."

Part IX. A series of 16 vibrios, chosen on the basis of their variability, are here studied with the idea of elucidating some of the chemical changes which underlie dissociation. The variation and dissociation in these vibrios is ascribable to at least three factors : (1) Loss of specific carbohydrate, which is probably the chief basis for the transition from a smooth to a rough development. (2) Change in constituents as exemplified by a vibrio giving rise to a daughter strain in which the protein and carbohydrate " are both different from those of the parent." This daughter, rough, strain had changed its protein to that which is characteristic of water vibrios and had developed an entirely different type of specific carbohydrate, consisting of glucose units alone, from the specific carbohydrates of types I and II, which are galactose and arabinose respectively. (3) The displacement of one chemical type by another. This phenomenon consisted of a swinging alteration from one type of carbohydrate to another, for example from glucose to galactose and back again. It is obvious how serological reactions must change with alteration of this sort. "An anti-serum prepared against the strain, when one member was

in the ascendancy, might not agglutinate the strain at all when, after a few weeks or months, the other member had gained the upper hand." The same phenomenon appears to be manifest when "medusa-head" rough colonies gradually disappear and then reappear.

The authors set forth their six groups (*Bulletin of Hygiene*, Vol. 10, p. 271) of vibrios based on the combinations of two types of protein with three types of specific carbohydrate.

Study of four El Tor strains, included in the 16 test vibrios, provided interesting results. "They have been found to form a chemically distinct group, although one that is closely related to both the cholera vibrios (through the specific carbohydrate) and to the water-vibrios (through the protein)." *W. F. H.*

GARDNER (A. D.) & VENKATRAMAN (K. V.). **The Antigens of the Cholera Group of Vibrios.**—*Jl. Hygiene.* 1935. May. Vol. 35. No. 2. pp. 262–282. [25 refs.]

The importance of this thorough-going re-examination of the cholera group question will be obvious to anyone who is working on the subject. Suspicion, it is said, had arisen that the agglutinating sera provided for diagnosis of the cholera vibrio were not sufficiently specific. If these sera contain antibody common to *V. cholerae* and related organisms, this would account for recent findings of an "incredibly high proportion of healthy carriers." It may also happen that supposedly single cultures giving rise to more than one "type" may in reality be mixed cultures. Important work which is being done at present on polysaccharide and protein components of vibrios is not yet final and complete, but affords a classification not quite in accord with serological classification.

Very clear indications are given of the technique used by the authors in their separation into groups of about 100 races of cholera and cholera-like vibrios from a variety of sources. For the serological differentiation the suspensions were of (1) H-O type, veal broth cultures, incubated 24 hours and killed with 0·2 per cent. formalin and 0·2 per cent. chloroform, and (2) O type, 24-hour agar cultures in salt solutions, placed in boiling water for 2 hours. The antisera also were of two kinds: (1) H-O sera made by injecting rabbits intravenously with the formalinized unheated suspensions; and (2) pure O sera made with the saline agar suspensions boiled for 2 hours. Absorption tests were done with either living or boiled suspensions. The biochemical reactions resulted in vibrios being described as typical, atypical or non-fermenting. By a "typical" vibrio the authors mean "producing acid without gas in glucose, mannite, maltose, saccharose; giving the cholera red reaction and not fermenting dulcite." The "atypical" vibrio diverges somewhat from the typical but has a general similarity to it, while the "non-fermenting" vibrio is one which fails "to acidify any of the carbohydrates mentioned" and exhibits other differences. Under the heading "cholera group" vibrios "typical" and "atypical" vibrios are included, but "non-fermenting" are excluded. Antigenic stability under long cultivation is assumed with these exceptions: (1) that change from inagglutinability on isolation to agglutinability immediately after seems not uncommon; and (2) that the rough variation involving the loss of the smooth O antigens need only be considered when "sufficiently pronounced to be detectable in ordinary

cultures." Rough antigens have not been investigated except to confirm the fact that "rough forms, if motile, have the common H antigen and are deficient in specific O component."

Another subject which has not been fully investigated is the effect of the very numerous bacteriophages that act upon *V. cholerae*, but the work done gives the authors "no reason to suppose that transmutation of species occurs under bacteriophage action." Again they reject the theory as not proven that, "*V. cholerae* (typus epidemicus) is transformed by the bacteriophage at the end of epidemic outbreaks into a disequilibrated form (typus endemicus) which has temporarily lost its epidemic potentialities and gained the power of haemolysis."

The results of cross agglutination reactions, in which O sera and unheated suspensions were used, give—with the addition of the characters biochemical similarity and possession of a common H antigen—the working scheme advocated by the authors for classification of their cholera group vibrios into subgroups, which they regard as entitled to the denomination species. The cholera group of vibrios in this scheme consists of: (*a*) an O subgroup I containing (1) non-haemolytic (goat cells) cholera vibrios of types original, variant and middle, and (2) haemolytic (goat cells) El Tor vibrios of types original and variant (? middle); and (*b*) O subgroups II, III, IV, V, VI and individual races (mostly haemolytic) which are paracholera, cholera-like and some El Tor vibrios. All the standard stock cholera vibrios received from various laboratories fell into subgroup I as did also most of the haemolytic vibrios called "El Tor." The other subgroups contained several vibrios and the residue was made up of single vibrios, each with a different specific O component.

Some important notes are given by the authors under the heading "heat-labile (H) antigen," such as that: (1) all their vibrios conforming to the cultural and biochemical standard of *V. cholerae* possessed a common H antigen; (2) absorption of an H-O serum with homologous O suspension removed all agglutinins for O suspensions of all species, leaving the common H agglutinin intact; (3) absorption of an H-O serum with an H-O suspension of a different O subgroup removed the H agglutinin for all species, leaving the O agglutinin intact; (4) the H component may possibly not be completely identical in all species; (5) those vibrios differing widely from the cholera group in biochemical characters did not show the common H antigen of the group.

Some consideration is paid to a non-specific antigen demonstrated by the action of O sera on boiled suspensions and it is indicated that the non-specific O reaction is explainable in one of two ways, either that the common flagellar (H) antigen is changed by heat into a new common antigen, or (2) the boiling destroys the H and brings out a common component, which has been inert in the unheated vibrio. The first hypothesis is ruled out. One final remark will attract attention: "The term 'agglutinable' in so far as it refers to the use of sera containing the non-specific H agglutinin must clearly be discontinued. All the official diagnostic sera hitherto in use have been of this type."

At the risk of making a long summary too long we add some of the authors' own conclusions: (1) The heat-stable antigens are divisible into: (*a*) a considerable number of specific antigens, best demonstrated by O sera and H-O suspensions, which serve as a basis of classification into O subgroups; and (*b*) a non-specific component

demonstrable with O sera and O suspensions. (2) The first subgroup contains all the standard cholera vibrios from central laboratories and is considered to be the only class of vibrios known for certain to cause epidemic cholera. (3) The haemolytic "El Tor" vibrios are serologically diverse and the term should be reserved for those with the same specific O component as the standard cholera vibrios. (4) For the identification of the undoubted cholera vibrios a standard subgroup I O-serum is recommended in conjunction with the haemolytic test and this should contain both the main and the subsidiary antigens of the subgroup. (5) As a working rule it is suggested that bacteriological proof of "cholera" or a cholera carrier should rest on the isolation of a non-haemolytic vibrio with the specific O antigen of subgroup I. *W. F. H.*

SCHOLTENS (R. Th.). Analyse des récepteurs du vibrion cholérique et du vibrion El Tor. [**Cholera Vibrio and El Tor Receptors.**]—*Acta Leidensia* (*Scholae Med. Tropicae*). 1934. Vol. 9. pp. 222–231. [Summary appears also in *Bulletin of Hygiene.*]

The subject matter of the author's analysis of cholera and El Tor vibrio receptors was extracted in this *Bulletin*, Vol. 31, p. 312. We may give here his conclusions: (1) Some sera agglutinating the cholera vibrio contain two agglutinins which are active to high titre. (2) One of these agglutinates all the vibrios and was called agglutinin A. The other agglutinates only a third of the vibrios and was called agglutinin B. (3) Both cause the same sort of flocculation. (4) Only those strains which are agglutinated by both agglutinins give rise to the two. (5) One strain although agglutinated by agglutinin B did not give rise to it on inoculation into the rabbit. (6) Both receptors are thermostable. (7) Both immunological types were found side by side. (8) Both immunological types were found among the so-called El Tor vibrios. In this respect the El Tor vibrios are identical with the cholera vibrios. *W. F. H.*

VASSILIADIS (P. Ch.). Activité des hémolysines des vibrions cholériques et El Tor. [**Haemolysins of the Vibrios of Cholera and El Tor.**]—*C. R. Soc. Biol.* 1935. Vol. 119. No. 18. pp. 332–334.

——. Hémolysines des vibrions cholériques vrais. [**Haemolysins of the True Cholera Vibrio.**]—*Ibid.* pp. 339–341.

i. The author has already shown that the true, non-haemolytic cholera vibrios are transformed into haemolytic strains by culture in glucose media. Some further research has been made into this question of the influence of culture media on the production of haemolysins. It has been found that growth in liquid media and serial subculture stimulate the production of haemolysins.

ii. The evidence for haemolytic power may be indirect and given by the antihaemolysin produced by antigenic compounds of the various vibrios. Rabbits were injected with filtrates of vibrio cultures and the serum obtained was anti-haemolytic. Moreover it was discovered that the ordinary anti-cholera agglutinating serum of the laboratory neutralized the El Tor haemolysin at the same titre as the anti-haemolytic serum to El Tor vibrios. *W. F. H.*

SCHOLTENS (R. Th.). Sur l'hémolyse du vibrion cholérique sous l'influence du bactériophage. [**Haemolysis of the Cholera Vibrio under the Influence of Bacteriophage.**]—*C. R. Soc. Biol.* 1935. Vol. 119. No. 25. pp. 1023–1025.

A secondary culture of the cholera vibrio on agar was used to inoculate (isolated colonies) 15 tubes of bouillon containing 0·5 cc. sheep blood. These cultures all showed growth on the following day. Those of flocculent growth gave a slight but definite haemolysis while the haemolysis with those of diffuse growth was almost negligible. Haemolytic cultures proved to be resistant and non-lysogenic.

W. F. H.

LINTON (Richard W.), SINGH (Harwant) & SEAL (S. C.). **A Study of Vibrio Filtrates.**—*Indian Jl. Med. Res.* 1935. Apr. Vol. 22. No. 4. pp. 659–674. With 1 plate.

Schwartzman's phenomenon on which this study is concentrated is possibly anaphylactic. He made intracutaneous injection into a rabbit of 0·25 cc. of a filtrate of a young culture. This gave practically no reaction, but if it was followed by intravenous injection in 24 hours of 1 to 1·5 cc. of filtrate a severe and haemorrhagic reaction with necrosis appeared at the site of the former injection. The same occurs with filtrates of 20-hour agar cultures of vibrios. Of the fractions into which vibrios can be divided by extraction with acid alcohol "the 'A' fraction alone yields a constant and typical reaction" while "the whole vibrios and the 'B' and residue fractions are without sensitizing effect."

W. F. H.

BANERJEE (Dhirendra Nath) & DATTA (Sunil Krisna). Cholera Kidney. A Clinical, Biochemical and Functional Study.—*Jl. Indian Med. Assoc.* 1935. July. Vol. 4. No. 11. pp. 497–498.

LINTON (Richard W.). Une base chimique pour la classification et l'étude des variations des vibrions.—*Bull. Office Internat. d'Hyg. Publique.* 1935. June. Vol. 27. No. 6. pp. 1108–1120.

LINTON (Richard W.) & SEAL (S. C.). The Effect of the Use of Living or Dead Suspensions of Vibrios on the Agglutination Titre.—*Indian Med. Gaz.* 1935. Feb. Vol. 70. No. 2. pp. 68–70.

MANAKO (K.). Cholera and Cholera-like Vibrio. Parts IV & V. Variability of Cholera Vibrio.—*Jl. Oriental Med.* 1935. May. Vol. 22. No. 5. [In Japanese. English summaries pp. 79–80.]

MANAKO (K.). Cholera and Cholera-like Vibrio. Parts VI, VII and VIII. Variability of Cholera Vibrio.—*Jl. Oriental Med.* 1935. June. Vol. 22. No. 6. [In Japanese pp. 949–962. [11 refs.]; 963–975. [20 refs.]; 977–983. With 7 figs. on 2 plates; English summaries pp. 85; 86; 87.]

POLLITZER (R.). A Further Note upon Cholera and Related Vibrios in Shanghai Waters.—*Reports National Quarantine Service.* Shanghai, China. 1934. Ser. 5. pp. 61–69. With 2 graphs.

REPORTS NATIONAL QUARANTINE SERVICE. Shanghai, China. 1934. Ser. 5. pp. 185–220. With 1 chart.—Central Cholera Bureau in 1934.

VASSILIADIS (Pierre). Behavior of Cholera and El Tor Vibrios towards the Shwartzman Phenomenon.—*Jl. Infect. Dis.* 1935. July–Aug. Vol. 57. No. 1. pp. 118–120.

AMOEBIASIS AND DYSENTERY.

Amoebiasis.

Spector (Bertha Kaplan), Foster (John W.) & Glover (Nelson G.). *Endamoeba histolytica* **in Washings from the Hands and Finger Nails of Infected Persons.**—*Public Health Rep.* 1935. Feb. 8. Vol. 50. No. 6. pp. 163–165.

Seventy-four carriers of *E. histolytica* cysts were examined. Hands, débris under finger nails, and nail parings, were examined after defaecation and before hands were washed. Only 5 gave positive findings; 2 showed very few live *E. histolytica* large cysts; 1 showed very few dead *E. histolytica* large cysts; and 2 showed live small cysts. One man, a plasterer, showed a number of large cysts of free living amoebae.

Of these 74 washings 54 were cultured for *B. coli-aerogenes*, of which 15 were positive. These findings suggest that contamination of food by carriers of *E. histolytica* under the ordinary conditions of food handling rarely happens. *H. M. Hanschell.*

Iskandar (Fayek). **Post-Dysenteric Oedema in Children.**—*Jl. Egyptian Med. Assoc.* 1935. Feb. Vol. 18. No. 2. pp. 134–137. With 1 chart.

Post-dysenteric oedema in children is accompanied by a definite fall in blood proteins.

The rôle played by plasma proteins in maintaining the colloid osmotic pressure of the blood and preventing retention of fluid in the interstitial tissues is well known.

Ten children suffering from post-dysenteric oedema were selected, after thorough examination had excluded nephritis or pyelitis. Their blood proteins, and those of 10 healthy control children of about the same age, were estimated by the Kjeldahl method. Serum was used instead of plasma because the fibrinogen fragment in plasma proteins is small (0·3 gm. per cent.) and appears to play no part in maintaining fluid balance between blood and tissues; and, moreover, the oxalate added to the tube in which blood for plasma is collected causes plasma to dilute itself by abstracting water from the cells and thus may significantly reduce the plasma protein concentration. These estimations made it clear that the post-dysenteric oedema was accompanied by a definite fall in blood proteins. On treatment (high protein diet) disappearance of oedema was accompanied by simultaneous rise in blood proteins. Increased capillary permeability as a factor in this oedema cannot be excluded. *H. M. H.*

Bonne (C.). Over niet herkende amoebendysenterie bij lijders aan andere ziekten. [**Want of Recognition of Amoebic Dysentery in Other Diseases.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1935. Mar. 19. Vol. 75. No. 6. pp. 470–479.

A study of a dozen post-mortem reports from a first-class hospital revealed that the patients had died from some very serious illness

without recognition of the fact that they were at the same time suffering from amoebic ulceration. Further study of such cases has suggested to the author that amoebic dysentery, itself a serious disease, is not infrequently missed under such circumstances as the above and may itself be the actual cause of death. It may not have been possible to demonstrate the presence of amoebae in the stools during life. Examples of the types of serious disease in which this amoebic complication was found after death were :—aneurysm of the aorta and phthisis, cirrhosis of the liver, bronchiectasis and stone in the bladder, cancer of the uterus with metastases and vesico-vaginal fistula, gangrene of the foot with bronchopneumonia and ankylostomiasis, typhoid fever. It is a fact that, in the tropics, amoebiasis is not examined for as a routine practice and this ought to be done. The case is otherwise with respect to malaria, which no physician in the tropics is likely to ignore as a possible complication. In hospitals, too, the ritual of taking temperatures is strictly performed, but not the duty of recording the number of stools. The patient, moreover, may not be confined to bed and the record of this important symptom may have to depend on his own statement : constipation even may be the symptom and not diarrhoea. The material again which is chosen for microscopic examination may not be well chosen : it should be, if possible, a fragment of blood-stained mucus. Lastly the laboratory report when received may be negative, even when amoebae are present, for the technique of examination is delicate and may fail. The author is well aware that dysentery amoebae may be found in persons who have [apparently] a completely sound intestine and again that they may not be found even where the amoebic ulcers reach almost to the anus.

It is strongly advised that the physician in the tropics should be on the look out for amoebiasis just as he is always on the look out for malaria. *W. F. Harvey.*

Esposito (Giuseppe). Un caso non comune di amebiasi a localizzazioni multiple. [**An Unusual Case of Multiple Amoebiasis.**]—*Giorn. Ital. di Malat. Esot. e Trop.* 1935. July 31. Vol. 8. No. 7. pp. 170, 173–176, 179–181. With 3 figs.

The patient, a man of 35 years, gave a history that 14 months before coming under observation he had had an attack of diarrhoea with tenesmus and passage of blood and mucus for 3 weeks. This cleared up and for some months he was apparently well, returned to work and ate his customary food. Then there supervened an attack of fever with pain over the liver and later pain in the right side of the chest with cough and signs of bronchitis, and expectoration wine-coloured and streaked with blood. The liver area was swollen, dyspnoea very marked and X-ray revealed opacity of the right side of the thorax and upper part of the abdomen. Repeated exploratory puncture brought away 500 cc. or more of reddish-brown fluid. Emetine was given, later stovarsol and finally another course of emetine and the patient left hospital well, 40 days after admission. The diagnosis appears to have been made on clinical grounds and the result of treatment, for except for " some doubtful amoebae in cystic form " in the sputum on his arrival at hospital, amoebae were never found and experimental injection of kittens *per rectum* with the fluids extracted by puncture of the pleura and the liver proved negative. [The title of the paper therefore rather begs the question.] *H. H. S.*

Wu (T. T.) & Chi (C. K.). **Amebiasis of Uterine Cervix. Report of a Case.**—*Chinese Med. Jl.* 1935. Jan. Vol. 49. No. 1. pp. 69–73. With 2 plates. [14 refs.]

The amoebae in this case were found in sections of cervical necrotic tissue obtained by biopsy. The amoebiasis of cervix was probably preceded by chronic cervicitis. Mode of infection uncertain; no history of dysentery; no rectovaginal fistula; no stool examinations.

H. M. H.

Akashi (Kazuyoshi). **The Treatment of Amoebiasis with Iodochlorhydroxyquinoline.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1934. Dec. Vol. 33. No. 12 (357). [In Japanese pp. 1801–1806. English summary p. 156.]

The author treated 15 cases of acute amoebic dysentery and 5 *histolytica* cyst carriers with vioform with uniform success.

It was given by mouth, in tablet or powder, 0·75 gm. daily for 15 days. The dysentery cases were well in a week and no relapse has occurred in a period of 1–5 months. All the carriers also were cured after three days of treatment. *A. G. B.*

Millischer (P.). Essai de traitement de l'amibiase intestinale par l'acide iodo-oxyquinoléine sulfonique. [**Treatment of Amoebic Dysentery by Mixiod.**]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 99–103.

The report is favourable.

The author states that he has had first hand and satisfactory experience of emetine and stovarsol therapy in over 2,000 cases of amoebiasis; and it is with that partisan bias that he approached the trial of Mixiod (acide iodo-quinoléine-sulfonique) in amoebic dysentery. Observations on 22 cases lead him to conclude that Mixiod is most effective when given simultaneously by mouth and as rectal lavage. As compared with emetine its action is more definite and rapid on cyst carriers than on infections with trophozoites. In the latter Mixiod may entirely replace emetine where the latter is contraindicated although its action is slower and treatment must be more prolonged. Emetine dosage may be reduced if given with Mixiod. *H. M. H.*

Akashi (Kazuyoshi). **The Treatment of Amoebiasis with Gavano.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1935. Feb. Vol. 34. No. 2 (359). [In Japanese pp. 189–194. English summary p. 194.]

Ten cases of acute amoebic dysentery were treated with gavano, which proved "remarkably effective"; in the case of 3 carriers progress was slow.

The drug was given by mouth, and by injection in two cases. In the dysenteries after 2–3 days the number of motions was reduced and pain disappeared. After 3–4 days *E. histolytica* could not be found. No relapse occurred in 3–6 months. In the carriers cysts disappeared on the 7th, 8th and 9th days. There was no evidence of toxicity. Gavano is said to be a derivative of ipecacuanha [see this *Bulletin*, Vol. 31, pp. 282 and 652]. *A. G. B.*

AGRIKOLANSKI (N.) & TIBURSKAYA (N.). **On the Treatment of Amebiasis with Osarsol.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1935. Vol. 4. No. 1–2. [In Russian pp. 16–18. English summary p. 18.]

The authors report the results of treatment of 15 cases of amoebic dysentery with "Osarsol" (=Stovarsol=Spirocide). The drug was administered three times a day in the course of four days, the doses being 1+1+2 tablets (0·25 gm. each) on the first two days, and 2+2+2 on the last two days (=20 tablets or 5 gm. "Osarsol"). The patients underwent 5–6 such courses with intervals of 6–7 days between them, with the result that a complete cure was effected in 11 cases. In two cases the treatment failed to expel the amoebae, while two others relapsed. *C. A. Hoare.*

AFRICA (Candido M.) & GARCIA (Eusebio Y.). **Iodaseptine Cortial (Iodobenzomethylformine) in the Treatment of Chronic Amebiasis.** —*Jl. Philippine Islands Med. Assoc.* 1935. June. Vol. 15. No. 6. pp. 305–311. [12 refs.]

Symptoms, and cysts and trophozoites, disappeared in five cases of treated chronic amoebiasis after intramuscular injection of iodaseptine cortial. All had been subjected to other forms of treatment without success.

Iodaseptine cortial, or Iodobenzomethylformine, is a French patented preparation primarily designed for the treatment of pulmonary tuberculosis and chronic rheumatism. The five cases are described. There were no special dysenteric symptoms, only chronic diarrhoea alternating with constipation and pain and with loss of weight and strength. In every case cysts were found but trophozoites in one only. After "two series" or a few injections of the drug the symptoms disappeared and did not recur. In one instance cysts were absent three years later, in another 12 months. The authors suggest that a further trial is justified. *A. G. B.*

NOSSINA (V.). **Action of Drugs upon** *Entamoeba histolytica in vitro.*—*Med. Parasit. & Parasitic. Dis.* Moscow. 1934. Vol. 3. No. 6. [In Russian pp. 451–459.]

The author studied the effect of emetine and yatren upon the dysentery amoeba cultivated in a fluid medium (John's combined with Barrett and Smith's media). Emetine has a slight action in an acid medium but the effect increases as the reaction approaches neutrality. At pH above 6·8 emetine kills the amoebae in a dilution of 1 : 5,000,000. Further rise in alkalinity does not increase the effect of the drug. The effective range of yatren is between pH 5·6–7·8 in a concentration of 1 : 5,000. *C. A. Hoare.*

BERETERVIDE (Juan Jose) & GRAU (Carlos A.). Una nueva sal de emetina : el canfosulfonato de emetina. [**The Camphosulphonate, a New Salt of Emetine.**]—*Prensa Méd. Argentina.* 1935. Apr. 3. Vol. 22. No. 14. pp. 671–681. With 12 figs. [12 refs.]

The authors claim for the camphosulphonate of emetine the advantages that the depressing action of the base, emetine, is counteracted by

the acid radicle ; that experiments carried out with frogs, rats, rabbits, guineapigs, cats and dogs have shown it to be only one-third as toxic as the hydrochloride ; that clinically patients show greater tolerance for the new compound than for the older ; and, finally, that it should replace the older.

The authors give an account of the preparation of Reychler's camphor-B-sulphonic acid (C_{10} H_{15} O. SO_3 $H)_2$, and of the emetine base and lastly of the compound. In testing the new drug, they find that the toxic action is due to the contained emetine and that it is a cardiac and central nervous system poison, and that, as stated above, the toxicity is only one-third of emetine hydrochloride. The dose employed in human subjects was 6 cgm. daily injected till 1·2 gm. had been given, *i.e.*, the course lasts for 20 days.

The two cases reported in detail are not very convincing of its efficacy. Both were cases of liver abscess with chocolate-coloured pus [but faecal examination in each case was negative for Entamoeba and none is mentioned as being found in the discharge]. Both were operated upon and in spite of injection of the new salt into the abscess cavity and of courses of it till the total mentioned, 1·2 gm., had been administered, in each case the abscess re-formed and more pus was removed at the second operation than at the first. To each patient three series of the injections were given before the condition cleared up. They were under treatment for 5 and 8 months respectively. [Since 6 cgm. is the usual dose of the hydrochloride, perhaps better and more rapid results might have been obtained with larger doses of the new compound since its toxicity was only one-third that of the hydrochloride.] *H. H. S.*

FAUST (Ernest Carroll), SCOTT (L. C.) & SWARTZWELDER (J. C.). **Influence of Certain Foodstuffs on Lesions of** *Endamoeba histolytica* **Infection.**—*Proc. Soc. Experim. Biol. & Med.* 1934. Dec. Vol. 32. No. 3. pp. 540–542.

KAGY and Faust 1930, and Faust and KAGY 1934, showed that raw liver and liver extract were distinctly beneficial to dogs suffering from acute amoebic enteritis and ventriculin consistently harmful to them [*ante*, pp. 190 and 191]. Faust discovered that dogs resistant to amoebic infection on a balanced diet could usually be infected if fed on canned salmon.

In the present experiments, 26 healthy young dogs were inoculated intracaecally (Faust 1931) with the same human strain of *Endamoeba histolytica*. All suffered from acute amoebiasis of a few days' standing when the tests were made. Fresh pigs' liver, ventriculin (Parke Davis & Co.) and commercial canned pink salmon (grade B) were the foodstuffs employed. One dog died, the other 25 were sacrificed.

Liver : 150 gm. unchopped raw liver fed to one dog daily ; clinical improvement ninth day : killed 13 days later, only few small shallow amoebic lesions in caecum and rectum. 60 gm. finely chopped liver in liver juice produced clinical improvement on 5th day ; killed 3 days later, only few shallow lesions in rectum. When only 12 gm. liquid and solid fractions of finely chopped liver had been introduced into large intestine of 3 dogs, 2 showed improvement on 4th day, one failed to improve ; autopsy revealed only few lesions in rectum of one dog ; numerous shallow lesions in large intestine of the other two. 60 gm. liquid and solid fractions of finely chopped liver given intracaecally daily procured marked improvement on third day ; and on sacrifice 2 days later only a very few pinpoint

lesions were found. Finely chopped liver autoclaved at 17 pounds pressure for 20 minutes and 60 gm. given daily orally (2) and intracaecally (2); all 4 dogs became rapidly worse; sacrificed on eighth day; multiple lesions throughout large intestine, many motile amoebae in lumen and in lesions. Chopped liver heated to 70°C. for 30 minutes to coagulate proteins; solid fraction doubly filtered and washed, fed orally, 85 gm. daily, to each of 2 dogs; liquid fraction (250 cc. solution from 100 gm. raw liver) given orally to each of 2 dogs; all 4 sacrificed on 22nd day. Solid fraction fed dogs revealed numerous deep undermining lesions, no healing; liquid fraction fed dogs revealed only very few small shallow lesions with extensive healing.

Ventriculin: 10 gm. suspended in 100 cc. water was given daily, orally to one dog, and intracoecally to 2 dogs; in all 3 infection became rapidly fulminating; on sacrifice, 2 on 9th day, one on 12th day, multiple deep lesions throughout large intestine in each, and in one a general inflammatory condition. Ventriculin 6 gm. in 50 cc. water, autoclaved (17 pounds pressure, 20 minutes), given daily orally to 2 dogs, intracaecally to 2; in all four improvement occurred and on sacrifice on 9th day relatively few active lesions were found.

Salmon, unaltered canned, was used routinely to exacerbate mild, chronic, or inactive infections. When macerated and given intracaecally the dog noticeably improved; on return to oral administration infection promptly fulminated. Peptic and tryptic digests of salmon given intracaecally daily (30 cc. containing 25 gm. canned salmon) caused rapid fulmination of infection; sacrifice on 10th day revealed large intestines studded with amoebic lesions.

Liver and ventriculin (15 gm. each suspended in 100 cc. of water daily); and liver and salmon (15 gm. each daily) were combined and given intracaecally. In the former experiment the liver failed to counteract effect of ventriculin; but in the latter marked clinical improvement and recovery were effected; and on sacrifice on 12th day, no amoebae and no unhealed lesions were discovered. *H. M. H.*

DESCHIENS (R.). Modification de l'aptitude pathogène, pour le chat, de l'amibe dysentérique en culture. [**Change in Pathogenicity for the Cat of Cultures of the Amoeba of Dysentery.**]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 119–126.

Eight strains of amoebae (all to start with haematophagous) have been studied—3 strains from France (autochthonous), 3 Moroccan, one Indo-China, one Madagascar—for pathogenicity to cats.

The strains were cultured in a medium containing rice starch, and the cultures maintained from three to eleven months. From two to four kittens were inoculated with each of the strains in culture. Of these 8 strains, originally virulent, 6 appeared to have lost their pathogenicity for the kitten, after culture in presence of rice starch; 2 maintained their pathogenicity, for which the duration of culture might account, as the 2 had been in cultivation less than three months, and the 6 for more than three months.

The author states that profound modification of the initial intestinal flora associated with the dysenteric amoeba, fermentation of the rice starch forming butyric, lactic, and propionic acids, acid reaction of the culture medium, could explain decrease or loss of pathogenicity if it be admitted that a proper flora associated with the amoeba is necessary to provoke amoebic dysentery.

[It is to be noted how few were the kittens inoculated with each strain.] *H. M. H.*

MELENEY (Henry E.) & FRYE (William W.). **Studies of *Endamoeba histolytica* and Other Intestinal Protozoa in Tennessee: IX. Further Observations on the Pathogenicity of Certain Strains of *E. histolytica* for Kittens.**—*Amer. Jl. Hyg.* 1935. Mar. Vol. 21. No. 2. pp. 422–437. With 2 figs. [31 refs.]

The four strains of *E. histolytica* studied were maintained for nearly three years in culture on egg-Ringer medium, overlaid with horse serum-Ringer, and enriched with rice flour. The strains were tested at intervals during this period to determine pathogenicity for kittens. Similar experiments were made with seven other strains of *E. histolytica*. Twenty or more kittens were used in nearly all the series of experiments with each strain.

"In these series of experiments there was considerable variation in the percentage of kittens which became infected with each strain, but the average extent and intensity of the lesions remained fairly constant in all the series performed with each individual strain.

"The average degree of pathology produced by the two strains from the hill country of Middle Tennessee continued to be much less than that produced by the two strains from the bottom-land of West Tennessee.

"Experiments with seven other strains of *E. histolytica* are reported in which one series of twenty or more kittens was inoculated with each strain: one strain from a symptomless 'carrier' in Nashville showed a very low degree of pathogenicity. Two other strains showed an intermediate degree of pathogenicity. Four strains from Chicago all showed very high degrees of pathogenicity.

"These results corroborate our previous conclusion that it is possible to demonstrate by large-scale kitten experiments performed under uniform conditions that strains of *E. histolytica* of varying degrees of pathogenicity exist.

"The work has also demonstrated that some strains of *E. histolytica* maintain a constant degree of pathogenicity throughout a period of at least 3 years in artificial cultivation.

"Since even the least pathogenic strains which we have encountered produce lesions in some kittens, and since human beings may harbor potentially virulent strains without showing clinical symptoms, it is important that every person encountered in medical practice who is found to harbor *E. histolytica* should be treated with an amoebicidal drug."

H. M. H.

FRYE (William W.) & MELENEY (Henry E.). **Studies of *Endamoeba histolytica* and Other Intestinal Protozoa in Tennessee: VIII. Observations on the Intestinal Protozoa of Young Pigs and Attempts to produce Infection with a Human Strain of *E. histolytica*.**—*Amer. Jl. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 404–414. With 9 figs. on 1 plate. [11 refs.]

Ten young pigs were studied with reference to their natural intestinal protozoa.

Uninucleate amoebic cysts, 5 to 12 micra, were found in all. The authors describe them as having the combined characteristics of *E. polecki* and *E. debliecki*. Other natural intestinal protozoa found were Iodamoeba, Trichomonas, Chilomastix, Giardia, Balantidium, and a coccidium. Infections with Balantidium were eliminated by a single dose of heptylresorcinol (dihydranol). Carbarsone treatment permanently eliminated the *polecki-debliecki* amoebae from all of the pigs. Iodamoeba later reappeared in three pigs and Trichomonas in eight

pigs. All attempts to infect the pigs with a pathogenic strain of *E. histolytica*, either by direct injection into the ileum or by rectal injections failed, whether the pigs were on a normal diet, or on a high carbohydrate diet. *H. M. H.*

PAVLOFF (P.). Recherches sur la présence de kystes à quatre noyaux d'amibes dysentériques dans les excréments des porcelets. [**Four-nucleated Cysts of** *E. histolytica* **in the Excreta of Pigs.**]—*Ann. Parasit. Humaine et Comparée.* 1935. Mar. 1. Vol. 13. No. 2. pp. 155–160. [12 refs.]

It was announced by KESSEL that pigs in China harboured amoebae producing cysts with four nuclei and that these injected into kittens behaved like *Entamoeba histolytica*. An examination of a large number of pigs in France and Bulgaria has not revealed any such infection. Uninucleated cysts similar to those described by PROWAZEK, CAUCHEMEZ and others occur. *C. M. Wenyon.*

TANABE (Misao). **The Excystation and Metacystic Development of** *Entamoeba histolytica* **in the Intestine of White Rats.**—*Keijo Jl. Med.* 1934. Dec. 31. Vol. 5. No. 4. pp. 238–253. With 1 text fig. & 38 figs. on 3 plates. [12 refs.]

By feeding cysts of *Entamoeba histolytica* to white rats and making preparations from the intestinal contents at varying intervals the author has been able to follow the excystation process and the subsequent development of the excysted quadrinucleate amoeba. The findings agree in all essential respects with those obtained by DOBELL on cultures of this amoeba, which appears to be truly pathogenic to white rats. Three excellently executed plates containing 38 figures illustrate the author's findings. *C. M. W.*

GNEZDILOV (V.). Contribution à la biométrie et à la statistique des kystes d'*Entamoeba histolytica* e d'*Entamoeba hartmanni*. [**Biometrical and Statistical Study of the Cysts of** *E. histolytica* **and** *E. hartmanni*.]—*Rev. Microbiol., Epidémiol. & Parasit.* 1934. Vol. 13. No. 2. [In Russian pp. 137–148. With 4 figs. [31 refs.] French summary pp. 148–149.]

The author made a biometrical study, using statistical methods, of over 2,300 cysts of the dysentery amoeba from three human carriers. He arrives at the conclusion that there exist two groups of amoebae differing markedly in the dimensions of their cysts: the one with large cysts belongs to *E. histolytica* (or *E. dispar*), the other with small cysts belongs to *E. hartmanni*. Each group contains a number of strains or races characterized by different average dimensions of the cysts, viz., those measuring on the average 6·93μ, 7·2μ, 7·75μ, 7·99μ and 8·25μ represent the group with small cysts, while those measuring 11·66μ, 12·85μ, 13·25μ and 14·47μ represent the one with large cysts. The specific status of the rare cysts with intermediate dimensions (9–11μ) requires further elucidation. It is suggested that since the biological properties of *E. hartmanni* are unknown, forms with small cysts should be treated separately in all works dealing with the incidence of the dysentery amoebae. *C. A. Hoare.*

ZERTCHANINOV (L.). Sur la différenciation des kystes semblables à celles de l'*Entamoeba histolytica.* [**Differential Diagnosis of** *Histolytica*-**like Cysts.**]—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 3. [In Russian pp. 267–273. With 4 figs. French summary p. 272.]

In the course of a coprological examination of the population in the Ural Region the author found that all the amoebic cysts of the *histolytica* type were of the small or medium varieties, measuring from 5 to 12μ in diameter. In view of this fact, and because all the cases observed in this region were symptomless carriers, the author concludes that the infections are due to *Entamoeba hartmanni* and *E. dispar*, and not to *E. histolytica.* Apart from size he claims to be able to distinguish the first two forms from *E. histolytica* by the morphology of the vegetative or active stages and by the dimensions and amount of the chromatoid bodies. With a view to differentiating between *E. hartmanni* and *E. dispar* an examination was made of 5,136 cysts obtained from 25 cases, using statistical methods. The cysts were found to fall into two groups, those of the first, which are referred to *E. hartmanni*, have a diameter from 4·25 to 9·35μ (average 7μ) with chromatoid bodies in 75·5 per cent., while the cysts of the second group, referred to *E. dispar*, range from 7·5 to 14·45μ in diameter (average 10μ), and have chromatoid bodies in 40·6 per cent. of specimens. *C. A. Hoare.*

ABDEL SAYED (Ibrahim). Résumé de sa communication faite le 2 juin 1933 sur l'amibiase.—*C. R. Soc. Méd. et Hyg. Trop. d'Egypte.* Alexandria. 1933–34. 5th Year. Vol. 1. pp. 29–30.

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CHANG (Hsiao-Ch'ien) & CHOU (Shou-k'ai). Amebic Dysentery and its Sigmoidoscopic Diagnosis.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 2. pp. 433–439. [11 refs.]

FARMAKIDIS (C.). A propos de l'amibiase.—*C. R. Soc. Méd. et Hyg. Trop. d'Egypte.* Alexandria. 1933–34. 5th Year. Vol. 1. pp. 31–34.

FISCHER (Otto). Chronische Darmstörungen und Amöbeninfektion. (Ein Gutachten für die Kriegsbeschädigtenversorgung.)—*Muench. Med. Woch.* 1935. Feb. 28. Vol. 82. No. 9. pp. 336–338.

HARGROVE (M. D.). Review of 112 Cases of Amebiasis.—*New Orleans Med. & Surg. Jl.* 1934. Dec. Vol. 87. No. 6. pp. 359–362.

HEGNER (Robert). Absence of Tissue Invasion in Monkey Carriers of *Endamoeba histolytica.*—*Amer. Jl. Trop. Med.* 1935. Jan. Vol. 15. No. 1. pp. 41–43.

IKEDA (Kano). Roentgenologic Observations of the Colon in Amebic Dysentery with Report of Seven Cases Originating in Chicago.—*Radiology.* 1934. May. Vol. 22. No. 5. pp. 610–621. With 7 figs. [12 refs.]

KITABATAKE (Eitaro). Investigations on Amoebic Dysentery. II. Experimental Studies on Amoebic Dysentery in Rats. Part I. Amoebic Dysentery of Rats in the Acute Stadium. *Jl. Oriental Med.* 1934. Oct. Vol. 21. No. 4. [In Japanese pp. 623–652. With 1 chart & 6 figs. on 3 plates. English summary pp. 57–58.]

KITABATAKE (Eitaro). Investigations in Amoebic Dysentery. II. Experimental Studies on Amoebic Dysentery in Rats. Part II. On Amoebic Dysentery in Rats in Chronic Stadium as well as on the Significance of House Rats as Vectors of the Transmission of Amoebic Dysentery.—*Jl. Oriental Med.* 1934. Nov. Vol. 21. No. 5. [In Japanese pp. 827–842. With 7 figs. on 3 plates. [31 refs.] English summary pp. 90–91.]

KUBO (Michio). Investigations of Amoebic Dysentery. IV. Experimental Studies on Amoebic Dysentery in Dogs. First Report. Amoebic Dysentery of Dogs in Acute Stadium.—*Jl. Oriental Med.* 1934. Dec. Vol. 21. No. 6. [In Japanese pp. 987–999. With 9 figs. on 3 plates. [15 refs]. English summary pp. 113–114.]

MATHIS (C.). Morphologie et cycle évolutif de l'amibe dysentérique.—Reprinted from *Algérie Méd.* 1931. May. 16 pp.

MÜHLENS (P.). Folgezustände und Fehldiagnosen nach Amoeben-Dysenterie und ihre Behandlung.—Reprinted from *Tung-Chi Med. Monatsschr.* 1934. No. 5. 12 pp. [In parallel Chinese.]

PATIÑO MAYER (C.) & GARCÍA ROBIN (Alfredo). Consideraciones sobre un caso de sigmoiditis amebiana crónica, de forma frustra. Resultado del tratamiento arsenical por vía rectal.—*Semana Méd.* 1935. Mar. 21. Vol. 42. No. 12 (2149). pp. 881–884. With 4 figs.

SABRI (Ismail A.). The Diagnosis of Chronic Dysentery in Children and the Use of the Sigmoidoscope.—*Jl. Egyptian Med. Assoc.* 1935. Feb. Vol. 18. No. 2. pp. 118–124.

SHATTUCK (George Cheever). Amebiasis in Boston.—*New England Jl. of Med.* 1934. Dec. 6. Vol. 211. No. 23. p. 1044.

SIMON (Sidney K.). The Clinical Aspects of Amebiasis.—*New Orleans Med. & Surg. Jl.* 1934. Dec. Vol. 87. No. 6. pp. 355–359.

TANGREDI (Gerardo). Anemia ipocromica grave da amebiasi intestinale.——*Policlinico.* Sez. Prat. 1935. July 1. Vol. 42. No. 26. pp. 1290, 1293–1294. [10 refs.]

TSUGE (Yukio). Recherches sur la pyogramme entre la dysenterie amibienne et bacillaire.—*Jl. Oriental Med.* 1934. Dec. Vol. 21. No. 6. pp. 95–98. With 12 figs.

VASILESCU (C.) & PAPAZIAN (R.). Kystes hydatiques suppurés du foie, compliqués d'abcès multiples au foie et péricardite purulente.—*Bull. et Mém. Soc. Méd. Hôpit. de Bucarest.* 1935. Mar. Vol. 17. No. 3. pp. 40–48.

YAMAMOTO (Yoshio). Investigations in Amoebic Dysentery. V. On the Cultivation of *Entamoeba histolytica.*—*Jl. Oriental Med.* 1934. Nov. Vol. 21. No. 5. [In Japanese pp. 811–825. With 1 chart. [33 refs.] English summary p. 89.]

MALARIA.

BULLETIN DE L'OFFICE INTERNATIONAL D'HYGIÈNE PUBLIQUE. 1935. May. Vol. 27. No. 5. pp. 903–929.—Enquête sur les règlements ou prescriptions officielles pour préserver du paludisme les personnes qui se rendent dans des régions malariques: Grande-Bretagne (Colonies Britanniques), Allemagne, Etats-Unis, France (Colonies Françaises et Territoires sous mandat français), Congo Belge, Pays-Bas, Indes Néerlandaises, Italie, Turquie. [**An Enquiry into the Official Regulations and Instructions for protecting from Malaria Persons proceeding to Malarious Countries.**]

The inquiry showed that the counsel generally given to Europeans in different malarious countries was that they should take quinine as a preventive, and should protect themselves against mosquitoes by nets and by proofing their houses. The method of quinine prophylaxis most commonly recommended was a daily dose of 25 centigrams (4 grains), or more rarely 40 to 60 centigrams (6 to 9 grains). In Egypt, Italy and Turkey, the preventive dose of quinine is given on only two days—consecutive or not—in the week. According to the Malaria Commission of the League of Nations, this method is not so efficacious as a small daily dose. The period over which the governments of different countries recommend their subjects to continue taking prophylactic quinine differs in different parts of the world. Europeans in British West Africa are recommended to take quinine daily during the whole of the time they are in Africa, and to continue it for 6 months after their return to England. In French Africa, prophylactic quinine is taken between May and September only. In the Dutch East Indies, quinine is continued for only 2 to 4 weeks after returning to Europe. On German ships, quinoplasmine is used as a prophylactic in preference to quinine. As recent work in England has shown that atebrin is a more potent and less risky prophylactic than plasmoquine, atebrin is to be tested on persons proceeding to West Africa in British ships.

W. Fletcher.

VAN CAMPENHOUT (Em.). La prophylaxie individuelle du paludisme au Congo Belge. [**Personal Prophylaxis in Belgian Congo.**]—*Bull. Office Internat. d'Hyg. Publique.* 1935. Feb. Vol. 27. No. 2. pp. 307–309.

Numerous laws are in force with reference to the prevention of malaria which deal with such matters as the provision of mosquito-proofing of houses, collections of stagnant water, accumulations of rubbish, the breeding places of mosquitoes and the like. Government officers are not compelled to take prophylactic quinine but, with rare exceptions, they do so. Medical history records of each officer are kept, and on these a note is made as to the regularity with which they have taken quinine. These records are considered in connexion with leave and pension. All officers on first appointment must attend 17 lectures on tropical hygiene and, during their service, pamphlets on the same subject are issued to them from time to time. Courses of instruction are also available for non-officials. All natives are treated without charge by the Government, and in certain native schools prophylactic quinine is administered regularly. *W. F.*

KOMP (W. H. W.) & CLARK (H. C.). **A Fourth Year's Observations on Malaria in Panama, with Reference to Control with Atabrine and Plasmochin.**—*Amer. Jl. Trop. Med.* 1935. Mar. Vol. 15. No. 2. pp. 131–154. [10 refs.]

This is an example of the comparative futility of voluntary drug control, among a native population living in an endemic area.

"During the past 5 years, 1930 to 1934, an area lying in the mid-basin of the Chagres River in Panama has been observed and studied with regard to malaria, and various sorts of treatment have been given the inhabitants in an effort to control the disease. . . . Malaria. . . . cannot be entirely eliminated, but by various means it can be reduced to negligible proportions, as is witnessed by conditions in the Panama Canal Zone, which lies within 7 miles of our towns. The costly measures of control used there are not economically feasible in our area, so our efforts have been directed toward a reduction of malaria, either by direct attack on the parasite by drugs, or by breaking the chain of infection in the mosquito by antigametocyte treatment. Our efforts have been concentrated on . . . the young children . . . We have used several drugs and combinations of drugs over the four-year treatment period. . . . It should be mentioned that all treatment was voluntary. . . . Various combinations of antimalarial drugs were used including quinine sulphate alone or with plasmochin, and atabrine alone or with plasmochin. None of the methods used were particularly successful in reducing the malaria rate, except possibly the combination of atabrine and plasmochin. Monthly surveys over four years indicate the presence of cyclical variations in malaria parasite rate extending over several years. If treatment of any sort happens to be given during a down-swing in rate, success is nearly sure to follow; but if it is given on an up-swing, apparently nothing can stop the natural course of the cycle. . . . Although we feel that the recent improvement in malaria parasite rate is not due solely to our efforts, we have no doubt but that the general health of our villagers is much improved over its condition in 1929, before our work started."

During the course of treating 400 persons with atebrin, no toxic symptoms of any kind were noticed. It was far different with plasmoquine and, when combined atebrin-plasmoquine treatment was given, cases of poisoning were sufficiently common to drive the authors to the conclusion that the toxicity of plasmoquine rendered it unsuitable for mass administration without medical supervision. This is seldom available except in experimental enquiries, and not always in these. The authors regret that it was not available. "Economic considerations overruled in the matter, as we could not afford the expense of maintaining the required supervision." *W. F.*

DE MELLO (Froilano). Une vue d'ensemble sur la chimioprophylaxie en masse des localités malariennes et ses résultats pratiques. [**Mass Drug Prophylaxis.**]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 87–92.

The results of mass drug prophylaxis are fairly good if the treatment is continued.

The author first tried the new synthetic drugs in hospital. The results were excellent and the relapses were few, but atebrin proved too expensive for field use. The next step was to try the effect of plasmoquine and quinine in a village. An isolated village was chosen, Paris green was used, adult mosquitoes were killed, the people were kept

under strict control, the drugs were given regularly, and everyone was thoroughly treated. The results were most striking. The spleen rate, in the next epidemic season, was reduced from 82 to 27, and, instead of half the population being incapacitated with malaria, there were only two cases. It would be impossible to impose such rigid discipline upon the general population and the next test was made upon a number of villages where no compulsion was used. Villages with a splenic index above 50 per cent. were given a primary 8-day treatment with plasmoquine and quinine, followed by a secondary treatment consisting of a daily dose and lasting for 12 weeks. Villages with a splenic index between 30 and 50 were given only the primary course. Many people failed to take the treatment, and the results showed that the primary treatment alone was useless. If effort, time and drugs are not to be wasted, it is not only necessary for the primary course to be followed by a secondary course, but the latter must be followed by fortnightly visits to the villages and the treatment of all relapses. *W. F.*

ISMAÏL (Assim). Mesures préventives contre le paludisme dans les régions palustres en Turquie. [**Preventive Measures against Malaria in Turkey.**]—*Bull. Office Internat. d'Hyg. Publique.* 1935. Feb. Vol. 27. No. 2. pp. 304–306.

Quinine prophylaxis is the method adopted for dealing with malaria, and when an area has been declared malarious by the Ministry of Health, certain regulations come into force under a law passed in 1926. The government supplies quinine for labourers on small holdings but, on farms where more than 15 persons are employed, the proprietor must supply 2 grams of quinine per week for each person. If he fails in this, the Health Department steps in and, if he does not pay the bill, he is liable to a fine and imprisonment. *W. F.*

DUKE (H. Lyndhurst). **Quinine as a Prophylactic in Malaria.** [Correspondence.]—*Lancet.* 1935. Mar. 9. pp. 572–573.

The author complains that in consequence of experiments made in Europe quinine has become discredited as a prophylactic against malaria in tropical countries. "The impression remains," he writes, "that without prophylactic quinine men go down with malaria more often than they used to do under the old rite of 5 grains a day." He does not consider that the results of experiments carried out with European strains of parasites, and with syphilitic patients who have never before suffered from malaria, should be applied to the treatment of patients in the tropics without further inquiry. He suggests that an investigation should be made in Uganda with European and native volunteers. *W. F.*

DECOURT (P.). Etudes sur la prophylaxie collective du paludisme. [**Mass Prophylaxis.**]—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 176–183.

The author has employed two schizonticidal drugs, quinine and atebrin (or quinacrine), and two gametocidal drugs, plasmoquine (or praequine) and rhodoquine. The objection to quinine was that it had to be given daily. The following doses of the other drugs were given :—Quinacrine 0·4 grams once a week. Praequine 0·03 grams once a week, or Rhodoquine 0·03 grams once a week. Smaller doses were given to children. The results were encouraging. *W. F.*

DECOURT (P.). Méthode mixte dans la prophylaxie medicamenteuse collective du paludisme. [**Mixed Drug Prophylaxis in Malaria.**]—*Bull. Soc. Path. Exot.* 1935. Apr. 10. Vol. 28. No. 4. pp. 255–261.

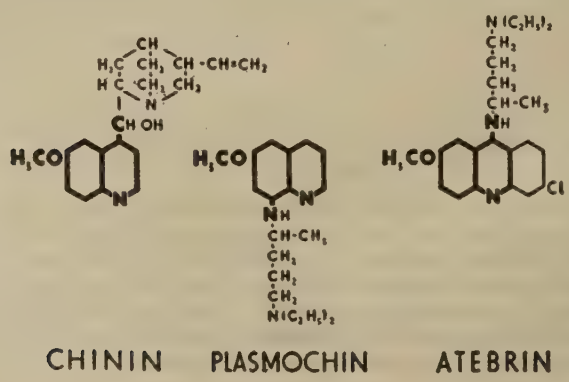
A prophylactic mass-treatment with quinacrine and praequine-rhodoquine, given once a week, is recommended. The prophylactic treatment should be begun as soon as the anopheles begin to breed at the commencement of the malaria season. If it is not begun then, and the population is already suffering from malaria, it is necessary to give a preliminary 5-day therapeutic treatment with quinacrine, combined on the first and on the last day with a gametocidal drug. A week later, the prophylactic treatment is begun. This consists of 0·3 grams of quinacrine and 0·02 to 0·03 grams of a gametocidal drug which may be praequine or rhodoquine or a mixture of the two. This treatment is given once a week, during or after food. The doses recommended for children and infants are shown in a table. The method was used with success in a district in the north of Tunis, not far from the Algerian frontier. *W. F.*

FARINAUD (M. E.). Les possibilités de l'atébrine en prophylaxie collective. [**Atebrin in Group Prophylaxis.**]—*Ann. de Méd. et de Pharm. Colon.* 1934. Oct.–Nov.–Dec. Vol. 32. No. 4. pp. 552–559.

This is a review of observations which have been made—particularly in Malaya by GREEN, WALLACE and KINGSBURY—on the use of atebrin as a prophylactic. In an editorial footnote it is stated that the names "atebrine" and "quinacrine" denote the same drug. The author concludes that on account of the danger of cumulative toxic effects, atebrin should not be placed at the disposal of an ignorant public, but should be given only under medical supervision. He suggests that Europeans are more sensitive to some synthetic drugs than members of coloured races. *W. F.*

SCHULEMANN (W.). **The New Synthetic Drugs.**—*Indian Med. Gaz.* 1935. Feb. Vol. 70. No. 2. pp. 83–88. With 2 charts. [73 refs.]

This lecture was delivered by the author in the Istituto di Malariologia in Rome. The following diagram of the structure of the three drugs was shown and the lecturer said, "A glance at Chart I will show



you that atebrin, plasmochin and quinine are all derived from 6-methoxy-quinoline which in atebrin is changed to acridin by combining it with a benzol nucleus. The side chains in atebrin and plasmochin are identical, alike in structure and in the nature of the linking member. The positions of the side chains on the ring system differ in plasmochin and quinine, but are analogous in quinine and atebrin." [See HENRY and GRAY, p. 385.]

The author does not consider that final conclusions should be drawn from the results of the treatment of artificially infected syphilitics. These patients are usually infected by the bites of a large number of heavily infected mosquitoes—doses of parasites far greater than they would receive in nature. It might be inferred from the work of CIUCA on general paralytics, and from that of SWELLENGREBEL on very heavily artificially infected volunteers, that the combination of plasmoquine with quinine did not affect the relapse rate ; but it has been found at the malaria treatment centre at Kasauli in India, that the relapse rate, which was 70 per cent. with quinine treatment, was reduced to 8·5 with plasmoquine and quinine ; eventually the treatment centre was closed for lack of patients. Atebrin does not reduce the relapse rate to quite the same extent as quino-plasmoquine, it is therefore necessary to combine atebrin with plasmoquine, or to give a short course of plasmoquine after the atebrin; in view of the abdominal pains which often occur when the two drugs are given together, the latter course is to be preferred. The author recommends the following treatment for the acute attack (first infection and relapse).

5 to 7 days—0·3 gm. (4½ grains) atebrin daily.
3 to 4 days—interval.
3 to 5 days—0·03 gm. (½ grain) plasmoquine daily.

For prevention (general prophylaxis) he recommends 0·02 gm. (⅓ grain) plasmoquine on two days in every week throughout the malaria season. Plasmoquine should not be taken on an empty stomach. The rare cases of fatal poisoning have not been due to variations in the toxicity of different samples. AMY has shown that fluctuations in the toxicity of plasmoquine do not occur. "Atebrin does not affect the liver in any way and does not give rise to jaundice." [See DE LANGEN and STORM, *ante*, pp. 726–8.] *W. F.*

CHOPRA (R. N.), GANGULI (S. K.) & ROY (A. C.). **On the Relationship between the Quinine Concentration in the Circulating Blood and Parasite Count in Monkey Malaria.**—*Indian Med. Gaz.* 1935. Feb. Vol. 70. No. 2. pp. 62–65.

There is no direct relationship between the concentration of quinine in the blood and the number of parasites.

These experiments were carried out on *Silenus rhesus* monkeys infected with *Plasmodium knowlesi*. Quinine was given both intravenously and intramuscularly. The maximum concentration was reached in about 20 minutes and remained fairly constant for about 1¼ hours. It was noted that though in some monkeys the maximum concentration was reached in half an hour and was maintained for some time, in others an equally high concentration never developed. The quinine had no visible effect upon the parasites in the blood, no matter how great its concentration. " The infection, as a rule,

was not controlled until 2 or even 3 injections were given at daily intervals, no matter what was the concentration of quinine in the blood. If any change in the parasites was observed, it was an increase in their number immediately after the injection, but never a marked decrease." When once the number of parasites approximated to one million per cmm. no amount of quinine, however administered, was of any avail in saving the monkey. *W. F.*

CHOPRA (R. N.) & GANGULI (S. K.). **Chemotherapeutic Studies on Plasmodium Infection in Monkeys. No. V. Action of Tebetren.**—*Indian Med. Gaz.* 1935. June. Vol. 70. No. 6. pp. 313–320.

" The drug, it seems, combines the virtues of atebrin and quinine." But the authors have omitted all reference to trials made elsewhere.

The authors treated with tebetren a number of *Silenus rhesus* which had been infected with *Plasmodium knowlesi*. They conclude that " in so far as the decrease in the number of parasites in the peripheral blood is concerned, tebetren appears to be intermediate in action between atebrin and quinine. . . . By the intravenous route, . . . its action resembles quinine. So far as relapses are concerned, the effects observed resembled more or less those produced in quinine-treated monkeys." *W. F.*

LANDEIRO (Fausto). Anreicherungsmethode für die Untersuchung der Malariaparasiten im Blute. [**Enrichment Method for the Detection of Malaria Parasites in the Blood.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. June. Vol. 38. No. 6. pp. 253–255.

In the course of the author's work on the sedimentation speed in malaria he used the sediment of the special pipette (Leitz) and the Westergren process for making preparations at different levels of the sedimented blood corpuscles. Parasites were counted in the usual thick drop, in the drops obtained by this process, and also in drops obtained from the lower part of the sediment in the mixing tube of citrate and blood. The drops were examined after an hour's sedimentation.

He examined 117 specimens thus, of which 57 were negative and 60 positive. The parasites stained better and were on a brighter and clearer ground than in the usual drops.

The lower part of the pipette sediment gave preparations 8 times as rich in parasites as the thick drop, the middle part 6 times as rich and the upper part 4 times as rich, while the lower part of the mixing tube sediment gave preparations 6 times as rich as the thick drop. *A. G. B.*

SINTON (J. A.). **A Method for cleaning the Capillary Tubes used for the Enumeration of Malarial Parasites in the Blood.**—*Records of the Malaria Survey of India.* 1935. Mar. Vol. 5. No. 1. pp. 1–2.

Capillary vaccine tubes are recommended in place of ordinary capillary pipettes for counting parasites by Sinton's method. If the tubes are thrown away after being used once, this is rather expensive. A method of cleaning them with nitric acid, water and alcohol is described. *W. F.*

KERIM (M. Abdel). **The Thick Drop Method in the Diagnosis of Malaria.**—*Jl. Egyptian Med. Assoc.* 1935. Apr. Vol. 18. No. 4. pp. 232–237.

The percentage of positives was increased from 67, found by the thin film method, to 95·5 found by the thick film method. The average time taken in finding parasites was 8·47 minutes in thin films, but only 38 seconds in thick films. *W. F.*

HOFFMANN (W. H.). Nachweis von Malariaparasiten in schlecht gelungenen Blutausstrichen. [**Demonstration of Malaria Parasites in Badly made Blood Smears.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. May. Vol. 39. No. 5. pp. 216–217.

In the case of bad blood smears, especially those that are too thick, the author advises that only the thinner part be fixed with methyl alcohol and that the whole smear be stained with dilute Giemsa. The unfixed part, thus freed from haemoglobin, becomes so transparent that even scattered parasites show up clearly. *A. G. B.*

MENON (T. Bhaskara), KRISHNASWAMY (T. K.) & ANNAMALAI (D. R.). **The Reticulocyte Count in Malaria and Kala-Azar and its Significance.**—*Jl. Indian Med. Assoc.* 1935. May. Vol. 4. No. 9. pp. 359–363. With 5 charts. [13 refs.]

Instead of the ordinary method of taking a drop of blood on to a slide smeared with saturated alcoholic cresyl blue, the authors take up in a pipette, one drop of a 1 per cent. watery solution of cresyl blue and one drop of blood, mix the two drops for half a minute, and then prepare films. In 10 cases of acute malaria, the average reticulocyte count was 1·06 per cent. ; in 7 cases of chronic malaria, 3·55 per cent. Cases of kala azar gave an average count of 3·62 per cent. When quinine was given to malaria patients, the count began to rise after 2 or 3 days, and continued to rise for another 2 or 3 days. *W. F.*

CHOPRA (R. N.), MUKHERJEE (S. N.) & SEN (B.). **Studies on the Protein Fractions of Blood Sera. Part III. Malarial Sera during and after the Rigor Stage.**—*Indian Jl. Med. Res.* 1935. Jan. Vol. 22. No. 3. pp. 571–580. [14 refs.]

The authors' summary is as follows :—

" During the rigor state in malaria the physical properties such as the pH and the buffer action change very little, while the relative viscosity and the surface tension are both lowered, the former to a greater extent than the latter.

" The protein fractions all deviate from the normal, albumin diminishes considerably, the euglobulin increases to a certain extent while the pseudo-globulin remains practically normal. The total proteins also diminish to a considerable extent. In those cases where the blood was drawn after the rigor had subsided the changes in the physical properties and also in the proteins are similar to those of the rigor cases but such changes are less marked and more towards normal.

" From these we are led to conclude that the changes in the physical properties as well as in the proteins of blood sera in malarial patients really set in during the rigor and reach a maximum when these changes begin to disappear and finally reach normal values within a short period after the rigor is over." *W. F.*

HENRY (A. F. X.). Mélanofloculation en dehors du paludisme et instabilité sérique. [**Henry's Reaction, Melanoflocculation without Malaria. Serological Instability.**]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 14. pp. 1443–1446.

The author discusses the occasional non-specific positive reactions occurring in diseases other than malaria.

Positive results have been reported in kala azar. KAROUT reported positive reactions in rabbits inoculated with typhus virus. His technique was not good; he did not employ formolized controls. TZECHNOWITZER and others reported positive reactions in typhus exanthematicus, but the patients came from malarious places and the typhus may have re-activated their serum. The author has had 4 positive results among 34 rabbits and guineapigs infected with typhus virus. The positive serums contained haemoglobin, and the reaction appeared to be associated with blood destruction. The same occurs, though rarely, in animals infected with trypanosomiasis. The reagents used in Henry's reactions possess certain properties of a colloidal nature which occasionally give reactions obscuring or simulating the specific reaction. The occasional reactions occurring in laboratory animals infected with parasites which destroy the blood cells and produce an instability of the serum do not vitiate the specific reaction which occurs in human malaria. *W. F.*

TRENSZ (F.). Technique de la sérofloculation palustre par la mélanine choroïdienne purifiée, rendue soluble dans l'eau distillée. [**Henry's Reaction with Soluble, Purified, Choroid Melanin.**]—*Arch. Inst. Pasteur d'Algérie.* 1935. Mar. Vol. 13. No. 1. pp. 11–38. With 1 chart. [14 refs.]

The melanin from the choroids of ox's eyes is dissolved in a warm alkaline solution. It is precipitated by acid and then redissolved by alkali. The process is repeated several times, until eventually the precipitate becomes soluble in cold water. This product is as active as the ordinary, untreated melanin, and has the great advantage of being stable. It can be kept for a long time and its activity is constant. In place of the distilled water and the 3 per cent. sodium chloride used by HENRY, the author employs 3 per cent. ammonium chloride, and only two tubes are needed for each test. As the reagent is quite clear, the results are easier to read. The soluble melanin is as sensitive as Henry's reagent, and it gives fewer positive reactions in non-malarial cases. *W. F.*

TRENSZ (F.). Sur les différences qualitatives qui existent entre les euglobulines du sérum de paludéens et les euglobulines du sérum normal, dans leurs rapports avec la sérofloculation palustre de Henry. [**Henry's Reaction. The Qualitative Difference between the Euglobulins of Normal and Malarial Sera.**]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 11. pp. 1076–1077.

It has been found that the melanoreaction of Henry depends upon an increase in the euglobulins of the blood. In certain diseases other than malaria the euglobulins are increased and the melanoreaction is positive. Sometimes, where the euglobulin is increased in non-malarious subjects, surflocculance occurs without melanoflocculation. The

author has separated the euglobulins from malarial and non-malarial sera by precipitation and dialysis. He has then dissolved them both in serum and in distilled water, and subjected them to Henry's test. As a result he concludes that there are qualitative differences between euglobulins. The euglobulin of malaria possesses a specific character which distinguishes it. (See TRENSZ below.) *W. F.*

i. TRENSZ (F.). Des relations qui existent entre les euglobulines et la surfloculation du sérum dans l'eau distillée. [**Henry's Reaction. Euglobulins and Surflocculation in Distilled Water.**]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 13. pp. 1332–1333.
ii. BENHAMOU (Ed.) & GILLE (R.). Les modifications sériques au cours de la malariathérapie.—*Ibid.* pp. 1334–1336.
iii. THIODET & RIBÈRE. Au sujet de la spécificité et du mécanisme de la réaction de Henry.—*Ibid.* pp. 1336–1338.

i. Surflocculance in distilled water is due to an instability of the serum and to this extent it is related to melanoflocculation, but the two phenomena are not identical. Melanoflocculation is not due simply to an increase of euglobulin, but to the presence of a special euglobulin. The changes caused by malaria are not merely quantitative, they are qualitative. Certain non-malarial sera which were rich in euglobulins gave a precipitate in distilled water, but not with melanin (*i.e.*, they were "negative"). Part of the precipitate was redissolved in salt solution, and part was added to normal serum. Henry's test was carried out, and again surflocculance occurred, while melanoflocculation was still negative although the euglobulin was increased. This procedure was repeated with the precipitate produced in a positive serum by distilled water. Here the redissolved euglobulin gave a positive Henry's reaction because it was malaria euglobulin.

ii. These authors contend that Henry's reaction is not due to a qualitative change in the euglobulin, but to its quantitative increase with reference to serum albumen and cholesterin. A negative malaria flocculation signifies that the flocculable albumen is maintained in colloidal solution by a sufficient quantity of colloid protectors represented by the serum-albumen and cholesterin. When there is a relative deficiency of these substances, flocculation occurs.

iii. Thiodet and Ribère consider that Henry's reaction is of questionable value and non-specific, and that it is due to euglobulin α which is increased in response to all kinds of antigens. A number of cases are cited where patients suffering from diseases other than malaria gave a positive Henry's reaction, for example: pernicious anaemia, lipoid nephrosis, starvation, duodenal ulcer, and several other diseases, nearly all associated with anaemia. *W. F.*

CHORINE (V.) & KOECHLIN (D.). Diagnostic du paludisme par mesure de l'instabilité du sérum dans l'eau distillée. [**Henry's Reaction. Diagnosis by Instability of Serum in Distilled Water.**]—*Bull. Soc. Path. Exot.* 1935. May 8. Vol. 28. No. 5. pp. 375–379.

The authors recommend that melanin should be abandoned and that the reaction should be carried out with serum and distilled water.

The results are read with a photometer. The reaction in distilled water shows that titres below 10 indicate the absence of malaria;

between 10 and 20, doubtful ; above 20 almost certain malaria. The reaction becomes negative 30 to 50 days after the institution of effective treatment. The reaction in a group of persons who had returned from malarious countries less than 6 months before being tested proved positive in 50 per cent. The number of positives decreased rapidly during sojourn in a non-malarious country, and fell to 5 per cent. in 2 years. The authors obtained like results when employing melanin, and they conclude that the reaction in distilled water is identical with the melanoflocculation reaction discovered by HENRY. (See pp. 130, 131, 420, 422, above.) *W. F.*

SINELNIKOW (S. I.), MOLDAWSKAJA-KRITSCHEWSKAJA (W. D.), GORCHOWA (E. L.), ALTHAUSEN (D. S.) & GRITZAY (A. A.). Vergleichende Bewertung der Melanoflokkulationsreaktionen mit nichterwärmten und auf verschiedene Temperaturen erwärmten Seren. [**Comparative Estimations of the Melanoflocculation Reaction with Unheated and Heated Sera.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. May. Vol. 39. No. 5. pp. 213–216.

An attempt to eliminate non-specific reactions in the melanoflocculation test by heating the serum to various temperatures.

The authors conclude that :—The melanoflocculation reaction carried out with, on the one hand unheated sera, and on the other hand, sera heated for 5 minutes to 54°C. gives concordant results in 85·4 per cent. of definitely diagnosed cases of malaria. If the heating is carried on, under otherwise similar conditions, for 20 minutes then the agreement is only 56·6 per cent. Sera heated to 45° or 50°C. for 5 minutes give the same results as unheated sera. In typhus fever cases, when the sera is heated to 54°C. for 5 minutes the reaction, when positive, is the same in heated and unheated sera, indicating a close connexion in the pathogenesis of malaria and typhus. The authors recommend that the method of carrying out Henry's reaction should be modified, and the sera should first be heated to 45°C. for 5 minutes, because in this method the full specificity of the reaction will be retained, but the possibility of a fallacious, non-specific flocculation will be eliminated. *E. D. W. Greig.*

SILVESTRINI (R.). Metodo facile di preparazione della sospensione di pigmento coroideo per la melanoreazione di Henry nella malaria. [**Easy Method of Preparation of Choroidal Pigment for Henry's Reaction.**]—*Policlinico.* Sez. Prat. 1935. Apr. 1. Vol. 42. No. 13. pp. 614–615. [13 refs.]

After describing in detail Henry's method of preparing the melanin for his reaction, certain modifications of it and the value and significance of the reaction, the author speaks of a method devised by him, which by its ease of preparation renders the test practicable for any medical practitioner. On the analogy of extraction of the pigment from melanotic tumours by trituration with ether, he suspends the choroidal pigment of the ox in, and treats it repeatedly with, ether in a funnel with a few cubic centimeters of physiological saline. The pigment is deposited in a layer between the saline and the ether. By carefully opening the tap of the funnel, the saline and pigment can be collected

and the ether discarded. Further grinding of the pigment in saline results in a finely opalescent suspension which is distributed in clean tubes and ready for adding to the different dilutions of serum for the test.

By its use the author has obtained marked flocculant precipitation with the sera of malaria patients after 2 hours at 37°C. *H. H. S.*

BENHAMOU (Ed.) & GILLE (R.). A propos du rôle de la cholestérine dans la mélanofloculation (réaction de Henry). [**Henry's Reaction. Cholesterin in Melanoflocculation.**]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 15. pp. 1573–1575.

Henry's reaction depends upon an increase of euglobulin, and a diminution of the cholesterin and serum albumen of the blood.

CHORINE and GILLE, on the contrary, found that if cholesterin were added to the serum the intensity of Henry's reaction was increased, and that if cholesterin were removed from the serum, by treatment with ether, it was decreased. The authors state that the added cholesterin does not increase the melanoflocculation, but it is precipitated by the addition of water to the serum, and so adds to the opacity. As regards the removal of cholesterin by ether, it is not a reduction in the amount of cholesterin which reduces the flocculability of the serum, but the presence of traces of ether, which act by lowering the surface tension. *W. F.*

KRITSCHEWSKI (I. L.) & RUBINSTEIN (P. L.). Ueber die Antigennatur des Melanins. [**Antigenic Structure of Melanin.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. Apr. 29. Vol. 84. No. 5/6. pp. 397–404.

An experimental study of the nature of the phenomenon of melanoflocculation (Henry).

In their investigations the authors employed birds infected with *Plasmodium praecox* and *P. cathemerium*. They obtained the melanin from the choroid of the eye of the ox. They consider that melanin is not a complete antigen, but a hapten and requires the addition of another substance (in the investigation the serum of the pig was employed) to convert it into a complete antigen. They consider that it is highly probable that the phenomenon of Henry in malaria is a reaction between the antigen and antibody and the melanin of the eye of the ox is, from the point of view of antigenic structure, identical with the melanin of protozoa (plasmodium). [SINTON & GHOSH consider that malaria pigment is a different substance from melanin. (See this *Bulletin*, Vol. 31, p. 706)]. As a result of their investigations the authors conclude that :—Melanin of the choroid is a hapten, which in the presence of an activator (Schlepper), serum of the pig, is converted into a complete antigen. Similarly the melanin produced by *Plasmodium praecox* is a hapten, whose antigenic completion is effected by an activator, the protoplasm of the protozoa. Henry's phenomenon in malaria is a reaction between antigen and antibody. Melanin differs from all other haptens in being insoluble.

E. D. W. Greig.

SAUNDERS (George M.) & TURNER (Thomas B.). **The Wassermann Reaction in Malaria.**—*Southern Med. Jl.* 1935. June. Vol. 28. No. 6. pp. 542–546. With 1 chart. [12 refs.]

The authors have investigated the Wassermann reaction in malaria, as many have done before, and they conclude that malaria does not cause fixation of complement in this reaction, but that it may stimulate a weak reaction and make it stronger. *W. F.*

ASCIONE (Guglielmo) & MARIOTTI (Ettore). Esperienze di trasmissione della infezione palustre coi filtrati di sangue e di liquido cefalo-rachidiano di malarici primitivi. [**The Transmission of Malaria by the Inoculation of Filtered Blood and Cerebrospinal Fluid.**]—*Riv. di Malariologia.* Sez. I. 1935. Vol. 14. No. 1. pp. 1–18. With 7 charts on 4 plates. [14 refs.] English summary.

Particulars are given of 9 experiments in which filtered blood or cerebrospinal fluid was inoculated into healthy individuals. In 5 cases out of 10, this was followed, after 10 to 15 days, by mild accesses of fever. Malaria parasites were not found, but quinine caused the malaria-like syndrome to disappear. [See this *Bulletin*, Vol. 30, p. 487.] *W. F.*

KNOWLES (R.) & BASU (B. C.). **Nuclear Division in Malarial Sporozoites.**—*Indian Jl. Med. Res.* 1935. Jan. Vol. 22. No. 3. pp. 443–447. With 1 fig. & 1 plate.

Examining sporozoites from the salivary glands of *Anopheles stephensi* infected with *Plasmodium vivax* and *P. falciparum* the author found that the chromatin as seen in dried films stained by Giemsa stain may be present as a single mass or as two or three masses which appear to arise by division from the single one. The appearance is interpreted as indicating nuclear multiplication in the sporozoite.

C. M. Wenyon.

MISSIROLI (A.) & MOSNA (E.). La reazione nucleare nei vari stadi di sviluppo dei parassiti malarici. [**Nuclear Reaction in Various Stages of Development of Malarial Parasites.**]—*Riv. di Malariologia.* Sez. I. 1934. Vol. 13. No. 5. pp. 553–558. English summary (5 lines).

Applying the Feulgen method of staining to human and avian malarial parasites the authors find that a positive result is obtained only with merozoites in the rosette stage and with the oöcysts and sporozoites in the mosquito. In all other stages there was a negative reaction. *C. M. W.*

IVANIĆ (Momčilo). Ueber die zwei allerfrühesten Kernteilungsstadien des Tertianaparasiten (*Plasmodium vivax* Grassi et Feletti) und deren Bedeutung. [**The First Two Stages of Nuclear Division of** *P. vivax.*]—*Zent. f. Bakt.* I. Abt. Orig. 1935. Feb. 18. Vol. 133. No. 5/6. pp. 274–282. With 11 figs. [13 refs.]

The author has studied the nuclear division in the schizonts of *Plasmodium vivax* fixed both by the dry and the wet methods. The

first two nuclear divisions are at first promitotic, it being possible to distinguish the linin spindle with chromatin granules arranged as an equatorial plate and polar bodies of a plastin nature. As division proceeds the polar bodies are dispersed, the division in its later stages becoming a true mitosis with a granule at each end of the spindle and daughter plates of chromatin substance. *C. M. W.*

FERREIRA (J. Chaves). Observações sobre os esporozoitos do *Plasmodium praecox* (*relictum*). [**Observations on the Sporozoites of** *P. praecox*.]—*Riv. di Malariologia.* Sez. I. 1934. Vol. 13. No. 5. pp. 559–562. With 35 coloured figs. on 1 plate.

The author has studied the structure of sporozoites of the bird malarial parasite *Plasmodium praecox* in the salivary glands of *Culex pipiens*. It appears that when they first reach the glands each has as a rule a single chromatin mass and a cytoplasm with a neutrophile reaction. During the course of the following 5 or 6 days it appears that the single chromatin mass divides into 8 smaller masses while the cytoplasm at first neutrophile acquires a basophilic and finally an acidophilic reaction. In the last case the sporozoites appear swollen, while the chromatin is disintegrated. *C. M. W.*

MISSIROLI (A.). Sullo sviluppo dei parassiti malarici. Nota 2a. [**Stages in the Life of the Malaria Parasite.**]—*Riv. di Malariologia.* Sez. I. 1934. Vol. 13. No. 5. pp. 539–552. With 4 text figs. & 24 figs. on 2 plates (1 coloured). [Refs. in footnotes.] English summary (8 lines).

Professor Missiroli as a result of experiments carried out with *P. praecox* (*relictum*) and canaries finds that sporozoites rapidly disappear from the site of inoculation, in 5–10 minutes in fact. Within the first 5 minutes some at least of the sporozoites will show a swollen nucleus in which are seen 4 or 5 chromatin granules distinct and separate one from another. If later examination, 3 hours or so after, reveals any of them they are only the degenerate or immature. The sporozoites break up into small fragments and are carried off by the lymphatics, in other words they may divide before entering the red corpuscles and do not always penetrate the corpuscle entire and then multiply as described in the text-books. *H. H. S.*

BLANCKENBURG (K.). Experimentelle Versuche ueber die Funktion der Blutreservoire bei Vogelmalaria (*Proteosoma präcox*). [**The Function of the Blood Reservoirs in Bird Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Mar. Vol. 39. No. 3. pp. 116–121.

It is well known that a large part of the blood of the body is retained in the organs (spleen, bone marrow, liver) as a reservoir where it is in intimate association with the reticulo-endothelial system. In cases of malarial infection large numbers of parasites occur in this reservoir and it would seem that, not completely destroyed by any drugs, they are the forms responsible for relapses. It occurred to the author that methods which bring about a reduction of the blood reservoir and an increase in the blood corpuscles in the peripheral blood might produce a corresponding increase in the malarial parasites. One of these is reduced atmospheric pressure and the author has demonstrated

that malaria infected canaries show an increase in the number of parasites in the peripheral blood if they are exposed to this condition for 5 to 10 minutes. *C. M. W.*

BRUMPT (Emile). Paludisme aviaire : *Plasmodium paddae* n. sp. du calfat (*Padda oryzivora*). Utilisation de ce parasite pour les recherches chimiothérapiques du paludisme. [*P. paddae* **of the Java Sparrow : its Value for Chemotherapeutical Researches.**]—*C. R. Acad. Sci.* 1935. Mar. 11. Vol. 200. No. 11. pp. 967–970. With 24 figs.

The Java sparrow which, as is well known, is frequently found infected with a halteridium (*Haemoproteus orizivorae*) is also liable to a less known plasmodium infection. The plasmodium was actually first seen by ANSCHÜTZ in 1909, who, finding its schizonts associated with the halteridium, thought that these represented an instance of the much talked of schizogony of the female gametocyte. This mistake was, in the author's opinion, again made by LEGROUX and LWOFF. The author and LANGERON studied the plasmodium in 1910 and noted its resemblance to *Plasmodium relictum*. It was not, however, inoculable to the canary or common sparrow. In the present paper the author records these original observations, not published before, and some further ones he has made recently. In spite of its resemblance to *P. relictum* he has not been able to inoculate it to any other bird but the Java sparrow. He gives a figure of the various stages of its development and proposes for it the name *Plasmodium paddae*. He thinks the plasmodium may prove to be useful for testing malarial therapeutic drugs as the Java sparrow is a much stronger bird than the usually employed canary. *C. M. W.*

BRUMPT (Emile). Paludisme aviaire : *Plasmodium gallinaceum* n. sp. de la poule domestique. [*P. gallinaceum*, **n. sp., of the Domestic Fowl.**]—*C. R. Acad. Sci.* 1935. Feb. 25. Vol. 200. No. 9. pp. 783–785. With 18 figs.

In 1912 PROWAZEK briefly referred to a malarial parasite of the fowl in Deli (Sumatra) which gave rise on reproduction to over 24 merozoites. No further reference to this parasite has been made unless the parasite noted by CRAWFORD (1933) in a number of imported fowls in Ceylon and identified by him as *Plasmodium relictum* (*praecox*) is the same species. In 1910 Dr. BROUSSAIS discovered a plasmodium in fowls in Indo-China and was able to inoculate it to other fowls. A film of the blood of an infected fowl was given to the author who now describes the parasite for the first time from this film. It is a large form producing distortion of the cell and displacement of the nucleus. The schizonts produce a variable number of merozoites (7–32), while the gametocytes are relatively large rounded bodies. This parasite, if it were rediscovered, would prove useful for therapeutic experiments. *C. M. W.*

MANWELL (Reginald D.). **Immunity to Cross-Infection in Avian Malaria due to** *Plasmodium vaughani*.—*Proc. Soc. Experim. Biol. & Med.* 1934. Nov. Vol. 32. No. 2. pp. 391–392.

In 1904 NOVY and MACNEAL described as *Plasmodium vaughani* a malarial parasite of the common robin. The author has isolated it in

canaries from a catbird in Syracuse, U.S.A., and has tested its immunity reactions towards other bird parasites. There does not appear to be any cross-immunity between it and other species, not even *P. rouxi* which it resembles morphologically, except that a pre-existing *P. praecox* infection may give a partial immunity to it. On two occasions infected birds seem to have rid themselves entirely of a *P. vaughani* infection, as evidenced by failure of massive doses of the blood to infect clean birds. This is a very rare occurrence in bird malaria. *C. M. W.*

MALAMOS (B.) & NAUCK (E. G.). Die Malariaplasmodien der Affen. [**Malarial Plasmodia of Monkeys.**]—*Zent. f. Bakt.* I. Abt. Referate. 1935. Apr. 18 & 25. Vol. 117. Nos. 9/10 & 11/12. pp. 193–218; 241–261. [2 pages of refs.]

In this article the authors give an exhaustive account of the malarial parasites of monkeys based on a detailed analysis of the literature, complete references to which are given. Not only are the parasites of the Old World monkeys dealt with, as in the recent publications of SINTON and MULLIGAN which are repeatedly referred to, but those of the New World are also considered, while the parasites of the higher apes are fully described. The article cannot fail to be of the greatest assistance to all who wish to study malaria as it occurs in monkeys. *C. M. W.*

MULLIGAN (H. W.). **Descriptions of Two Species of Monkey** *Plasmodium* **isolated from** *Silenus irus.*—*Arch. f. Protistenk.* 1935. Vol. 84. No. 2. pp. 285–314. With 2 charts & 2 coloured plates. [26 refs.]

Much of the information contained in this paper has already been published by the author in collaboration with SINTON. It gives, however, a descriptive account of *Plasmodium knowlesi* and *P. cynomolgi*, both of which together with *P. inui* (described by SINTON, see below) occur as natural infections in the monkey *Silenus irus* (*Macacus cynomolgus*). The paper is illustrated by two excellent coloured plates showing the characters of the two parasites. Some reference is also made to *P. inui*, and its cycle of development is given as 48 hours while in the later paper by SINTON, based probably on more extended observations, the figure is 72. *C. M. W.*

SINTON (J. A.). **A Quartan Malaria Parasite of the Lower Oriental Monkey,** *Silenus irus* (*Macacus cynomolgus*).—*Records of the Malaria Survey of India.* 1934. Dec. Vol. 4. No. 4. pp. 379–410. With 79 coloured figs. on 2 plates & 1 chart. [31 refs.]

The author describes the isolation in pure culture of a third malarial parasite from the monkey *Silenus irus*. Hitherto two species have been isolated, *Plasmodium knowlesi*, Sinton & Mulligan, 1932, with a 24-hour periodicity, and *P. cynomolgi*, Mayer, 1907, with a 48-hour cycle. The former produces a maximum of 11 merozoites, does not enlarge the red cell and produces a stippling demonstrable only by special staining, while the latter produces up to 16 merozoites, enlarges

the red cell and gives rise to conspicuous stippling. The new parasite, which has been identified with *P. inui*, Halberstadter & Prowazek, 1907, has a cycle of 72 hours, enlarges the red cell slightly, produces stippling which is less conspicuous than that caused by *P. cynomolgi* and produces up to 16 merozoites. These 3 malarial parasites occur naturally in *Silenus irus* very commonly in mixed infections. They do not produce any serious symptoms in the natural host nor do *P. inui* and *P. cynomolgi* in other species of *Silenus* to which they are inoculable. On the other hand *P. knowlesi* is highly pathogenic for *S. rhesus*, in which it gives rise to a severe disease often associated with haemoglobinuria. The *Silenus irus* in which the 3 parasites were found had come to India from Malaya. It appears that *P. inui* is identical with the parasite described by HALBERSTADTER & PROWAZEK (1907) from *S. irus* from Java and *S. nemestrinus* from Sumatra and Borneo and with the form seen by MATHIS & LEGER (1911) in *S. rhesus* and *S. lasiotis tcheliensis* from Tonking. Thus *P. inui* has a wider distribution than the other 2 species which at present are known only from Malaya.

The following table taken from the paper gives the differential characters of the 3 parasites.

	Pl. inui	*Pl. cynomolgi*	*Pl. knowlesi*
Natural hosts ...	*Silenus irus* *S. nemestrinus* *S. rhesus* *S. lasiotis tcheliensis*	*S. irus*	*S. irus*
Regions from which recorded	Borneo, Java, Sumatra, Tonking, Malaya	Malaya	Malaya
Duration of schizogony cycle	72 hours	48 hours	24 hours
Chromatin in young ring forms	Frequently double and of very unequal size	'Accessory dot' present	'Accessory dot' present
Trophozoites ...	Amoeboidicity of lobose nature; vacuolation marked up to early segmentation	Amoeboidicity marked, of '*vivax*' character; vacuole at first well developed but not marked in old forms	Amoeboidicity slight or absent; vacuole small in older forms
Pigment in trophozoites	Yellow to brown, becoming darker with age; appears early; fine and abundant with peripheral distribution	Golden-brown; appears later and is coarser and scantier than in *Pl. inui*; distribution less markedly peripheral	Golden-brown to almost black; appears early; abundant
Mature schizonts...	Maximum 16 merozoites. Often rosette	Maximum 16 merozoites. More irregular	Maximum 11 merozoites. Grape-like cluster

	Pl. inui	*Pl. cynomolgi*	*Pl. knowlesi*
Gametocytes ...	About size of normal red cell; pigment scattered, yellowish brown to brown and abundant	Distinctly larger than red cell; pigment not very abundant; darker than in *Pl. inui*	About size normal red cell; pigment relatively coarse, brown to black, and abundant
Infested red cells ...	Slightly enlarged with older forms. Stippling less conspicuous, scantier than with *Pl. cynomolgi*	Much enlarged with old forms. Stippling very conspicuous and dots very numerous	Not enlarged; showing characteristic distortion. Stippling only shown by special stains
Pathogenicity ...	Few or no symptoms. Easily inoculable to other species of *Silenus*. Not inoculable into higher monkeys	Usually no severe symptoms. Easily inoculable to other specimens of *Silenus*	Mild in *S. irus*, but causing very severe symptoms, often haemoglobinuria, when inoculated into *S. rhesus*. Has been transmitted to man and the gibbon

C. M. W.

KNOWLES (R.) & GUPTA (B. M. Das). **Latent Malaria Infection in Monkeys.**—*Indian Med. Gaz.* 1934. Oct. Vol. 69. No. 10. pp. 541–545. With 3 figs.

A specimen of *Silenus irus* on which splenectomy had been performed followed by inoculation with a pure strain of *Plasmodium knowlesi*, developed an intensive malarial infection in which not only the inoculated parasite but also *P. inui* var. *cynomolgi* was present. The operation of splenectomy appeared to have re-awakened a latent infection. To test the matter further a series of 5 young *Silenus irus* were subjected to careful examination. Thick and thin films were examined daily for 10 days. The result was the discovery of parasites in two. An attempt to arouse infection in the others by injection of 2 cc. of horse serum failed. Then 2 cc. of blood from each of the negative monkeys was inoculated into susceptible *S. rhesus*, with the result that one became infected, showing that one of the 3 negative *S. irus* had a very slight infection. The 3 monkeys were then subjected to splenectomy, with the result that malarial parasites appeared in the blood of all. It appears, therefore, that the most certain method of detecting a latent malarial infection is by splenectomy.

C. M. W.

NAUCK (E. G.) & MALAMOS (B.). Ueber Immunität bei Affenmalaria. [**Immunity in Monkey Malaria.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. Mar. 4. Vol. 84. No. 4. pp. 337–358. With 6 figs.

In the investigations described in this paper the author has followed the development of immunity in monkeys inoculated with *Plasmodium knowlesi*. Three different monkeys were used (*Silenus rhesus*, *S. irus* and *Cercopithecus mona*) and it was found that they differed from one another as regards reaction to the infection and the rate of development of immunity, which was of two types. That to develop first was a toxin immunity or an immunity which enabled the animal to tolerate the parasites present in the blood. Later there developed in addition to this a parasite immunity which enabled the animal to suppress the parasites by getting rid of them entirely or by keeping them in abeyance. Though from the point of view of the development of immunity the spleen is very important it is not absolutely necessary, for immunity will develop in splenectomized animals though more slowly than when this organ is present. The removal of the spleen in an already immune animal lowers the immunity to some extent. The existence of acquired immunity is not entirely dependent on the presence of a latent infection (premunition) since it may exist when, as tested by every available means, the monkey appears free from parasites. *C. M. W.*

CHAND (Khazan) & HARBHAGWAN. **Some Unsuccessful Attempts to transmit Monkey Malarial Parasites to Common Laboratory Animals.**—*Records of the Malaria Survey of India.* 1934. Dec. Vol. 4. No. 4. pp. 373–378.

An attempt to infect the rabbit, guineapig, rat, mouse, squirrel and dog with one or other of the three malarial parasites (*Plasmodium knowlesi*, *P. inui*, *P. cynomolgi*) of the monkey *Silenus irus* (*Macacus cynomolgus*) has completely failed. *C. M. W.*

PITTI-FERRANDI (François) & SAUTET (Jacques). Anophélisme sans paludisme dans un village corse de montagne. [**Anophelism without Malaria in a Corsican Mountain Village.**]—*Rev. Méd. et Hyg. Trop.* 1934. Nov.–Dec. Vol. 26. No. 6. pp. 262–267.

The village of Pietra-di-Verde with some 700 inhabitants is situated about 15 kilometres from the east coast of Corsica, at an altitude of 500 metres. It used to be malarious, but, since 1925, there has not been a single local case in spite of the continual importation of parasites by villagers returning from the plains. This change is not due to the deviation of the anopheles by an increase of domestic animals: there are fewer animals than in the past, and mules—the only ones which were stabled—have been largely replaced by motor transport. The larvae of *A. maculipennis* and *A. bifurcatus* are plentiful, but the adults do not come into the houses to feed, and people sleeping in rooms with open windows, close to the breeding-places, are never bitten. The mosquitoes probably feed on the domestic animals which are turned loose in the woods, for they are not plentiful in the stables. The local *A. maculipennis* appears to be a small, paucidentate race. One of the authors has carried out a vigorous quinine treatment of all cases of malaria for a number of years, and there have been fewer imported

cases, but these factors are not sufficient to account for the disappearance of the disease, because in neighbouring villages in the plains, where the same has been done, malaria has not disappeared. *W. F.*

i. TREILLARD (M.). Gîtes, sites ou régions, dans la localisation des espèces anophéliennes de l'Indochine méridionale. [**Breeding-places, Sites or Regions in the Localization of the Anophelines of Southern Indo-China.**]—*Bull. Soc. Path. Exot.* 1935. Jan. 9. Vol. 28. No. 1. pp. 40–42.

ii. ——. Tableau synoptique pour la détermination rapide des anophèles d'Indochine. 2. Larves. [**A Synoptic Table for the Rapid Determination of the Anopheles of Indo-China. 2. Larvae.**] —*Ibid.* pp. 42–44. With 1 fig.

i. The species of Anopheles having been identified, we need to know as definitely as possible where and when they are to be found. As yet, however, breeding-places cannot be determined precisely, since we are still ignorant of too many of the factors governing their selection by the female mosquitoes, and the subsequent development and fate of the progeny. The real characteristics which make a breeding-place attractive to female Anopheles do not necessarily affect its topography, and may be incommunicable by means of description or photographs. On the other hand no appreciable results have been obtained by studying either the microflora, microfauna or physico-chemical qualities of water, although recent investigations by MORIN and BADER (see this *Bulletin*, Vol. 31, p. 718) seem to indicate a suggestive simultaneity between certain percentages of carbonic acid and the presence of larvae of *A. minimus*. To avoid serious errors we must confine ourselves to broad categories (running and stagnant water, spring water and salt, water but slightly or heavily charged with organic matter, etc.), and to the idea of larger or smaller faunal regions, within which every collection of water is more or less suspect. Moreover it must not be forgotten that the biological needs of the adult are just as important as the physiological necessities of the larva.

ii. The table provided is on the lines of that recently given by the author for the adults of the species included (this *Bulletin*, *ante*, p. 438), but the characters are indicated in a purely schematic and conventional manner by means of blank or shaded spaces. Intended primarily for the use of beginners, this method of determination may have a certain value, but accurate results are unlikely to be obtained without practice, and larvae for examination will be better dead than alive.

In a list of twenty-one species of *Anopheles* met with in Indo-China between January and September, 1932, the following are shown as harbouring malaria parasites in the south :—*A. hyrcanus*, *A. minimus*, *A. aconitus*, *A. jeyporiensis*, *A. ludlowi*, *A. leucosphyrus* and *A. kochi*.

E. E. Austen.

GASCHEN (H.). Sur un nouvel agent transmetteur du paludisme en Indochine septentrionale *Anopheles culicifacies* Giles 1901. [*A. culicifacies* **as Malarial Vector in Indo-China.**]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 111–113. [10 refs.]

The presence of *A. culicifacies* in Indo-China was first notified in 1932 by TOUMANOFF and FARINAUD. The author captured a specimen in

1934 at Lahati (Yunnan) with oöcysts in the gut. It probably acts as a vector in the highlands and is responsible for the generalized malaria of mild type in such areas as the plateaux of Yunnan, where the only other anopheles are *A. sinensis* and *A. vagus.* *W. F.*

GASCHEN (H.). Recherches entomologiques dans la province du Yunnan. [**Entomological Investigations in the Province of Yunnan.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1934. Nov. Vol. 12. No. 9. pp. 873–892. With 1 folding chart. [14 refs.]

——. Faune entomologique des voies d'accès au Yunnan. [**Entomological Fauna of the Approaches to Yunnan.**]—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 194–198.

The province of Yunnan, situate in the extreme south-west of China, is a high plateau, traversed fan-wise by several mountain chains, and by large rivers running from west to east and south. Investigations into its anopheline fauna made by MORIN in January, 1934, were followed by others conducted by the author in the ensuing August and September. Eleven species of *Anopheles* were met with, viz. :—*A. sinensis, A. vagus, A. culicifacies, A. minimus, A. jeyporiensis, A. lindesayi, A. maculatus, A. aitkeni, A. barbirostris A. gigas* and *A. kochi*—all, with the exception of *A. lindesayi* of which adults alone were found, in both larval and adult stages. *A. culicifacies* and *A. gigas*, until encountered by the author, had not been taken in Yunnan ; a specimen of the former, caught at Lahati, contained oöcysts in the stomach-wall. In the vicinity of Yunnanfou *A. sinensis* was found breeding at an altitude of some 2,400 metres (nearly 8,000 feet).

Phlebotomus (*Ph. barraudi*) was captured in the province for the first time. *E. E. A.*

FENG (Lan-chou). **Notes on Some Mosquitoes collected from Shantung Province, North China.**—*Chinese Med. Jl.* 1935. Apr. Vol. 49. No. 4. pp. 359–365.

The author cites three papers about anopheles in Shantung, by CHRISTOPHERS, HINDLE and himself. He himself has made several collections of mosquitoes since 1927 ; they contain 15 species, 3 of which are anopheles, 4 aëdes and 8 culex. A short description is given of each with notes on their habits. *A. hyrcanus* var. *sinensis* is the most common anopheles both in the plains and hills and has been shown by HINDLE and Feng to be infectible with *P. vivax*. *A. lindesayi* var. *japonicus* is rare, and it is not known whether it bites man. *A. pattoni* is common in the hills and will harbour *P. vivax*. *A. G. B.*

PETRISHCHEVA (P. A.). Zur Fauna und Biologie der Culicidae des Karakala-Gebietes. [**Contribution to the Fauna and Biology of Culicids of the Karakala Region.**]—*Trud. Karakal. i Kzuil-Atreksk. parazit. Eksped. 1931 i Mater. po Faune Turkm.* in *Trud. Sov. Izuch. proizv. Sil*, Ser. turkmensk. Leningrad, Acad. Sci. 1934. Pt. 6. pp. 85–104. With 6 figs. & 1 graph. [In Russian.] [Summarized in *Rev. Applied Entom.* Ser. B. 1935. Mar. Vol. 23. Pt. 3. pp. 73–74.]

" The 15 species of mosquitos found in the Karakala region (south-western Turkmenistan) in 1930 included 6 of the genus *Anopheles, viz., A. superpictus*, Grassi, which was the most common, *A. maculipennis*, Mg., *A. claviger*, Mg. (*bifurcatus*, auct.), *A. hyrcanus* var. *pseudopictus*, Grassi, *A. pulcherrimus*, Theo., and *A. plumbeus*, Steph. The last three were

rare. Notes on the breeding-places are summarised in a table. Larvae of *A. superpictus* occurred from May till the end of November in almost all types of water, especially in spring water exposed to the sun, along the pebbly banks of rivers and streams, and in flooded areas with a very slow current and sparse vegetation. They were often found, together with those of *A. claviger*, in wells in which the water was very high, and in one instance larvae, pupae and empty pupal skins occurred in a deep well situated in a gloomy mine gallery. As the walls of the well were of hard rock and there was no vegetation, the author believes that the larvae of *A. superpictus* can develop on the colloid substances dispersed in water if coarser particles in suspension are absent. Larvae of *A. claviger*, which were found throughout the year, occurred in a variety of breeding-places, including water exposed to the direct rays of the sun, streams almost hidden in dense grass, and in one instance water from a sulphur spring devoid of macroscopic organic matter. Larvae of *A. maculipennis* occurred from May till the end of November in large shallow accumulations of water formed by the overflow of irrigation ditches and covered with grasses, and sometimes along pebbly river banks.

"The adults of *A. superpictus* were predominant in dwellings and out-houses, while *A. maculipennis* occurred much less frequently, and *A. claviger* very rare. On the whole, mosquitos were most numerous in gorges, caves and burrows of animals, reeds, etc., at a distance of from 6 to 25 miles from human habitations. *A. superpictus*, which was again predominant, was found at altitudes up to 6,500 ft., *A. claviger* up to 5,000 ft. and *A. maculipennis* up to 2,500 ft., while other Anophelines occurred in valleys up to an altitude of 1,600 ft. The adults of *A. superpictus* and *A. maculipennis* were found throughout the year, the former being most numerous in August and September. *A. claviger* was obtained from April to the end of November, *A. hyrcanus* var. *pseudopictus* from June to the end of August, and *A. pulcherrimus* in July and August only."

RUSSELL (Paul F.) & BAISAS (Francisco E.). **Habitats of Philippine Anopheles Larvae.**—*Philippine Jl. Sci.* 1934. Dec. Vol. 55. No. 4. pp. 297–306. With 5 plates. [15 refs.]

Although the genus *Anopheles* is abundantly represented in the Philippine Is., comparatively little is known of the bionomics of the local species, of which, to the extent indicated in the title, the present paper, "based on collections made by the staff of Malaria Investigations from January, 1930, to September, 1934, in every province in the Philippines under varying conditions as to altitude, type of breeding place, and time of year," provides a useful summary. In addition to original observations, earlier reports by other writers have also been utilized. The breeding-places of no fewer than twenty-seven species or varieties, two of which have not been precisely identified, are noted and in some cases illustrated. Breeding habits in the same species often vary widely, and on the other hand observed preferences are difficult to explain. *A. minimus* var. *flavirostris*, "the chief malaria vector in the Islands, . . . breeds particularly in foothill streams along the shaded edges, especially among bamboo roots." *E. E. A.*

SEN (Purnendu). **Anopheles Breeding in Relation to Rice Cultivation in Lower Bengal.**—*Records of the Malaria Survey of India.* 1935. Mar. Vol. 5. No. 1. pp. 97–108. With 8 charts. [12 refs.]

"Every area of cultivation must be judged on its own merits."

Certain municipalities prohibit cultivation within half a mile, or a mile, of their town or village, but this is not always necessary. Three

villages surrounded by rice fields, within 12 miles of Calcutta and typical of lower deltaic Bengal, were chosen for observation. Nearly 50 per cent. of the mosquitoes breeding in the rice fields were *A. hyrcanus* var. *nigerrimus* ; *A. culicifacies* was not found. *A. philippinensis* was found in some of the fields, but not in large numbers, and two other carriers, *A. varuna* and *A. annularis*, occasionally. One of the villages was malarious, with a spleen rate of 50 per cent. ; one was slightly malarious, with a spleen rate of 10 per cent. ; the third was healthy, and its spleen rate was nil. In this last village, the water of the paddy fields had a higher salinity, and *A. philippinensis* did not breed there. The author concludes that " It does not appear that there is any direct correlation between the malariousness of a place and rice cultivation in lower Bengal." *W. F.*

MEASHAM (J. E.) & CHOWDHURY (M. U.). **A Note on the Anopheline Mosquitoes of the Anaimallai Hills.**—*Records of the Malaria Survey of India.* 1934. Dec. Vol. 4. No. 4. pp. 363–365.

The Anaimallai Hills are the tea planting district of the western Ghats, 10 degrees north of the Equator. The estates lie at an elevation of 3,000 to 4,000 feet, surrounded by hills 5,000 to 8,000 feet high. *A. fluviatilis* was the only anopheline found to be infected ; it breeds in the grassy edges of slow-running streams where shade is not too dense. From June to October, the rivers are in flood and anopheles cannot be found in them. The malaria transmission season lasts from March to June and, during those 3 months, 8·86 per cent. of the *A. fluviatilis* were found to be infected. Counts were made of adults caught in stables and dwellings, which showed the androphilic character and prevalence of *A. fluviatilis*. These are some of the figures :—*A. fluviatilis*, 199 in dwellings, 4 in cattle sheds ; *A. maculatus*, 14 in dwellings, 34 in cattle sheds ; *A. vagus*, 12 in dwellings, 123 in cattle sheds. *W. F.*

i. EVANS (A. M.) & LEESON (H. S.). **The *Funestus* Series of *Anopheles* in Southern Rhodesia, with Description of a New Variety.**—*Ann. Trop. Med. & Parasit.* 1935. Apr. 25. Vol. 29. No. 1. pp. 33–47. With 10 figs. [12 refs.]

ii. LEESON (H. S.). **Another Anopheline of the *Funestus* Series from Southern Rhodesia.**—*Ibid.* pp. 69–71.

i. In Southern Rhodesia, what a few years ago would have been regarded simply as *Anopheles funestus* now proves to consist of :—*A. funestus* (*typicus*), *A. leesoni* (described in 1931 as a subspecies of *A. funestus*, but in this paper raised to specific rank), and a new variety here characterized as *A. funestus* var. *confusus* var. nov. The main distinctive characters of all three of these, in their different stages, are stated in the text, shown in tabular form and displayed in the figures. Notes on distribution in S. Rhodesia, and on bionomics are added. Adults of all three, which breed at the edges of sluggish streams and in swamps, occur in houses. Out of doors their favourite retreats along streams are among grass and weeds, in crevices and cavities in the soil, and beneath stones at " drifts " ; they likewise lurk in disused quarries and gravel-pits.

ii. *A. funestus* var. *rivulorum* var. nov., here described, is an addition to the foregoing. The egg has not so far been identified, but

the larvae, which in the shape and size of the main tergal plates resemble those of *A. longipalpis*, occur " in slowly moving streams near banks and among boulders," with those of *A. funestus* var. *confusus*, *A. leesoni*, *A. longipalpis* and *A. pretoriensis*. The adults are found " along streams, in crevices and cavities in the banks."

E. E. Austen.

AMBIALET (R.). Activité anophélienne et conditions climatiques sur le littoral algérien. [**Anopheline Activity and Climate on the Algerian Coast.**]—*Arch. Inst. Pasteur d'Algérie.* 1935. June. Vol. 13. No. 2. pp. 201–204. With 1 map, 1 chart & 4 figs. on 2 plates.

A village near Constantine with much malaria was selected for these trials. Traps of metallic gauze, such as are set in the apertures of doors and windows, baited with rabbits were arranged and were emptied twice a week for a year, while observations were made of maximum and minimum temperature, rainfall, fog, wind, etc. The result is shown graphically. In the traps were collected female *A. maculipennis* (and one male) and female *Culex pipiens*, which seemed to show that the insects entered for blood rather than shelter. The graph shows parallelism between captures of Anopheles and Culex and the importance of seasonal variations in the activity of mosquitoes. They were active at two periods—from May 26 to July 10 and from September 1 to November 20, *i.e.*, between the minimum and maximum of 10° and 30°. The great heat in summer was as inimical to them as the cold of winter.

A. G. B.

VILLAIN (Georges), DUPOUX (Robert) & MARINI (Charles). Contribution à l'étude de l'anophèlisme tunisien et aperçu de la lutte antianophèlienne dans la régence. [**Anophelism in Tunis, with Sketch of the Anti-Mosquito Campaign in the Protectorate.**]—*Arch. Inst. Pasteur de Tunis.* 1935. Apr. Vol. 24. No. 2. pp. 309–342. With 12 figs.

The first part of this paper consists of a list, in tabular form and in many cases giving details as to vegetation, etc., of *Anopheles* breeding-places in Tunis, all of which have been inspected and verified by the authors, while the larvae found have been carefully determined. The species met with are :—*A. maculipennis*, which occurs more or less everywhere ; *A. hispaniola* ; *A. multicolor* ; *A. algeriensis* ; *A. sergenti* and *A. superpictus*. *A. bifurcatus*, *A. marteri*, *A. broussesi* and *A. elutus*, although occurring in Algeria, have not so far been encountered. The importance of *wells* as anopheline breeding-places is emphasized ; but abandoned wells, or modern ones fitted with wind-pumps, are more dangerous than those of the Arab type, in which the water is frequently and violently disturbed by buckets.

A. maculipennis appears to show a marked preference for human blood, and GALLIARD (see below, p. 813) from an examination of eggs and larvae from various regions in Tunis, considers that all those collected belong to var. *labranchiae*. In winter, at least in certain specified regions, the adult females take refuge in houses and pass into semi-hibernation, *i.e.*, they remain active and ready to feed, but do not go outside in order to oviposit.

Anti-mosquito measures on a large scale, for which the necessary funds and personnel are now available, and of which some details are given, have been in operation in Tunis for scarcely five years. As regards biological control, very satisfactory results have been obtained from stocking with top-minnows (*Gambusia holbrooki*), which are among the most valuable auxiliaries in attacking anopheline larvae. Reliance is also placed on oiling, and Paris green, for the dissemination of which an aeroplane proved to be too costly in material, is employed only for broad, grass-grown expanses. *E. E. A.*

DUNN (Lawrence H.). **Entomological Investigations in the Chiriqui Region of Panama.**—Reprinted from *Psyche.* 1934. Vol. 41. No. 3. pp. 166–183.

The greater part of this paper is concerned with animal and bird parasites, but there are a few notes on mosquitoes (*Anopheles albimanus*, *A. punctimacula* and nine culicines), and on species of *Simulium* and Ceratopogonidae (*Culicoides* and *Lasiohelea*) attacking man. The majority of the culicines met with were found breeding, but no anopheline larvae were discovered. Specimens were collected on three different occasions, but the investigations appear to have lasted only a few weeks. *E. E. A.*

BOYD (Mark F.), CAIN (T. L.), Jr. & MULRENNAN (J. A.). **The Insectary Rearing of** *Anopheles quadrimaculatus.*—*Amer. Jl. Trop. Med.* 1935. May. Vol. 15. No. 3. pp. 385–402. With 7 figs.

This is a detailed description of the type of outdoor insectary used in Florida, and an indoor insectary in New York, for rearing *Anopheles quadrimaculatus* and *A. punctipennis.*

The same methods with very slight modifications serve for the two species; more extensive modifications are probably required for *A. crucians.* Photographs and plans of both insectaries are given. In Florida the natural conditions of temperature and humidity are satisfactory; in New York, by means of a Frigidaire air-conditioning unit, the temperature is kept always at about 72°F. (22°C.) and by introducing water vapour from the hot water supply, a relative humidity of about 70 per cent. is maintained. In the belief that ultra violet rays are essential to proper larval development, these are supplied two hours daily from a lamp. The larvae are reared in enamelled pans 12 inches in diameter and 2½ inches deep, and fed on hay infusion with strips of cork floating on the surface. The adults are fed on man. The many empirical details as regards the preparation of the hay infusion, etc., must be read in the original. Colonies of 3,000–5,000 are maintained. *V. B. Wigglesworth.*

BARBER (M. A.). **Malaria Studies in Greece. A Method of detecting the Eggs of** *Anopheles* **in Breeding Places and Some of its Applications.**—*Riv. di Malariologia.* Sez. I. 1935. Vol. 14. No. 2. pp. 146–149. English summary (5 lines).

A thumbless mitten or bag of white muslin is worn on the left hand. The surface of the water is skimmed with a pan and the contents of the

pan are strained through the mitten. The material collected on the mitten is examined with a hand lens. A good combination of lenses for field use is a 7X and a 20X. If it is desired to take eggs to the laboratory, several mittens can be used, or squares of muslin may be employed to place over the glove. The mittens, or the squares, can be put into flat boxes with the eggs on them for transport to the laboratory.

W. F.

RICE (J. B.) & BARBER (M. A.). **Malaria Studies in Greece. A Modification of the Uhlenhuth-Weidanz Precipitin Test for determining the Source of Blood Meals in Mosquitoes and Other Insects.** —*Jl. Lab. & Clin. Med.* 1935. May. Vol. 20. No. 8. pp. 876–883. With 6 figs.

This is a detailed account of the test illustrated with photographs and diagrams. It should be read by those who wish to carry out precipitin tests on mosquitoes.

The authors obtained precipitating sera for man, sheep, horse, pig and cow in ampoules from the Istituto Sieroterapico of Milan, Italy. These were diluted with seven parts of the following diluent :—

Sodium chloride	4·25	gram
Glycerine	166·00	c.c.
Phenol	2·50	,,
Distilled water	330·00	,,

The diluted sera will keep 10 months, overlayed with paraffin in the ice-box. One cubic centimetre of undiluted serum is sufficient for the testing of 700 mosquitoes. The fresher the blood to be tested the better. The blood inside a mosquito often becomes black and unfit for the test in 24 hours if the weather is hot. The authors put their collections of mosquitoes in corked, labelled test-tubes ; the tubes are placed in a large thermos jug with abundance of ice for transport to the laboratory. It is best to remove blood from the mosquito to filter-paper on the same day, but, with a well-iced thermos jug, this may be postponed for 24 hours. Round, hard, filter-paper, 9 cm. in diameter (Whatman No. 5) is used. The mosquitoes are lightly chloroformed, and the blood from each stomach is expressed on to the margin of the filter-paper ; labels are written in the middle. Dried blood specimens can be kept for months in a cool, dry place. Each blood spot is cut out for testing, and dissolved in 3 cc. of salt solution. The blood spots are allowed to soak in the salt solution for an hour at room temperature in order to extract the serum. The actual tests are made in capillary tubes, 6·5 cm. long with an internal diameter of 2 mm. A description is given of the manipulation of these tubes and of the method by which they are cleaned.

W. F.

MISSIROLI (A.). Osservazioni sulla biologia dell'*Anopheles plumbeus.* I Nota. [**On the Biology of** *Anopheles plumbeus.* **Preliminary Note.**]—*Riv. di Malariologia.* Sez. I. 1935. Vol. 14. No. 2. pp. 150–154. With 2 figs. English summary.

The author states that the " negative phototropism " of larvae of *A. plumbeus* is known and that the same avoidance of light guides the

adult in selecting the site for depositing her eggs. He found numerous larvae in shaded cavities in rocks where clean rainwater was collected, but from other collections fed by springs and exposed to light they were absent. He agrees with ROUBAUD that the larvae of winter generations possess a remarkable reserve of fat and develop slowly regardless of the environmental conditions. *H. H. S.*

PUNTONI (V.). Sur le développement des larves d'anophèles dans les eaux d'égout. [**The Development of Anopheline Larvae in Sewage.**]—*Boll. Sezione Ital., Soc. Internaz. di Microbiologia.* Milan. 1934. May. Vol. 6. No. 5. pp. 161–164.

——. Azione delle acque di fogna sullo sviluppo delle larve anofeline. —*Riv. di Malariologia.* Sez. I. 1934. Vol. 13. No. 6. pp. 721–733. French summary.

In view of the general belief that anophelines, as opposed to culicines, need clean water for their development, the author set himself to determine whether irrigation with sewage would be likely to prove a useful method in a campaign against the former. Unfortunately the outcome of his experiments, in which he used larvae of *Anopheles maculipennis*, vars. *labranchiae* and *messeae*, and various dilutions of sewage as media, appears to show, not only that there is no foundation for the popular idea in question, but also that the employment of sewage as a fertilizer would actually accelerate Anopheles-breeding, and would increase the proportion of larvae which arrive at maturity. *E. E. Austen.*

MEHTA (Dev Raj). **Effect of "Saline and Free" Ammonia on the Oviposition of** *Anopheles culicifacies* **and** *Anopheles subpictus* (*rossi*).—*Records of the Malaria Survey of India.* 1934. Dec. Vol. 4. No. 4. pp. 411–420. With 1 chart. [20 refs.]

The author wishes to define the concentrations of ammoniacal materials which prevent the oviposition of two common Indian Anophelines.

The greater part of the work was done in cages containing vessels holding natural waters of different ammonia concentration, or else solutions of ammonia salts prepared in the laboratory. The "saline and free" ammonia was measured by a simplified Wanklyn process. If we understand the author aright, there were several different waters or solutions in each cage, so that the numbers of eggs collected is a measure of the insects' preference. Gravid female Anopheles were introduced in considerable numbers, generally 20–30 per cage. The experiments were repeated a number of times and the results show clearly that (in cages) *A. culicifacies* will lay eggs freely in concentrations up to about 6 parts of free ammonia per million. The upper limit for *A. subpictus* is higher, and this species appears to avoid water with less than 1 part p.m. when other waters are available.

A few observations were made on the ammonia concentration of water in which larvae of these two species were found in nature, and the more extended work of SENIOR-WHITE is considered. It seems that in the field the upper limit for *A. culicifacies* is very much lower than in the laboratory. [We should be disposed to continue the cage experiments, using fewer females per cage (so as to exclude any possible

effect of overcrowding) ; a dish of distilled water in each cage would provide a good control. It would also be advantageous to study the distribution of the eggs of species of Anopheles in nature, if the prevalent species are capable of being identified by their eggs.]

P. A. Buxton.

HACKETT (L. W.) & MISSIROLI (A.). **The Varieties of *Anopheles maculipennis* and their Relation to the Distribution of Malaria in Europe.**—*Riv. di Malariologia.* Sez. I. 1935. Vol. 14. No. 1. pp. 45–109. With 4 plates. [66 refs.]

—— & ——. Les variétés d'*Anopheles maculipennis* et leur relation avec la distribution du paludisme en Europe.—*Medicina Países Cálidos.* Madrid. 1935. Jan. Vol. 8. No. 1. pp. 1–60. With 23 figs. [65 refs.]

This is an excellent review of the subject illustrated with tables, photographs and drawings, together with Appendices giving details of the methods of collecting eggs, examining them and sending them by post.

" It is now clear that *A. maculipennis* is not a homogeneous species, but a collection of widespread varieties." In 1920 ROUBAUD suggested that there were two races of *A. maculipennis*, one with many teeth which fed on animals, and another with few teeth, which fed on man. According to ROUBAUD, in regions with well-stabled cattle, competition favours the insects with strong dental armatures fitted for piercing the tough hides of animals, and so a zoophilic race becomes differentiated. Where such conditions do not exist, undifferentiated *maculipennis* remain and continue to bite man. An average maxillary index of 14–15 is an indication of differentiated zoophilism ; populations with an average maxillary index below 14 are malaria carriers.

FALLERONI was the first to give names to any of the varieties of *A. maculipennis* ; he noted, in 1924, that the eggs of the anopheles from the Pontine marshes were of two kinds, grey and dark. In 1927, he proposed the name " *messiae* " for the form with the dark, barred egg, and the name *labranchiae* for the form with the grey dappled egg. The *labranchiae* in the south had a lighter egg than those in the north. In the same year, van THIEL showed that the " short wings " and " long wings " of Holland were valid races, and gave the name *atroparvus* to the former. *Atroparvus* has been shown to be identical with the dark grey egged northern *labranchiae*, and therefore the latter name is now restricted to the southern variety with the lighter egg. The generally accepted varieties are :—

maculipennis, Meigen, or *typicus* ; egg with 2 simple bars.
messeae, Falleroni ; egg dark (barred).
melanoon, Hackett, ; egg uniformly black. Possibly a form of *messeae*.
atroparvus, van Thiel ; egg dark grey dappled.
labranchiae, Falleroni ; egg light grey dappled.
elutus, Edwards ; egg uniformly grey.

These varieties are identified by (*a*) the egg marking and the character of the floats ; (*b*) the larval hairs ; (*c*) the external harpaginal spine of the male adult. A table is given showing the morphological difference between the six varieties. The authors are of opinion that " the egg-types provide the only satisfactory method of dividing *A. maculipennis*

into a number of constituent forms, with a minimum of overlapping." Roubaud's maxillary index, and the wing-length classification of van THIEL have statistical value only ; they are useless in the classification of individuals and have only a local validity, *i.e.*, the long wings in one country may be no longer than the short wings in another ; the longest wings found in Italy are half a millimeter shorter than the shortest wings of North Europe. The number of teeth of *atroparvus* averages more than 17·5 in Germany and Holland, while it does not reach 16 in either *atroparvus* or *messiae* in Italy.

The subdivision of *A. maculipennis* into varieties on the ground of differences in the eggs is supported by biological differences in (*a*) the selection of breeding-places, (*b*) sexual behaviour, and (*c*) winter habits. *Atroparvus* breeds in saline water, *messiae* in fresh ; *atroparvus* will copulate in a closed space (" stenogamy "), the other varieties will not ; *atroparvus* does not go into complete hibernation, the other varieties do. The validity of the classification is further supported by (*d*) the constancy of the egg characters in a given variety ; (*e*) the constancy of the morphological and biological characters of the adults bred from a given type of egg ; and, finally, (*f*) " attempts to cross mate the different forms have so far revealed a barrier of sterility between them which is the strongest evidence of their specific nature."

The relation of the different varieties to malaria.—All the varieties of *A. maculipennis* are equally susceptible to malaria and, though some prefer to feed on animals, there is never an insurmountable barrier, either microclimatic or instinctive, between any of the varieties and man. In almost the whole of northern Europe *A. maculipennis* lives at the expense of domestic animals, and man is said to be protected from malaria through " deviation " of the anopheles by animals. In the malarious regions of southern Europe, *A. maculipennis* bites man persistently. The principal reason for the difference in its behaviour, in the north and the south, is that the anopheline population of the latter regions consists of varieties such as *elutus* and *labranchiae* which prefer to feed on man. For example, at Diamantina on the river Po, *elutus* occurs mixed with more northern races of *A. maculipennis* ; 226 *elutus* were caught there in stables and 158 in houses ; while, of the other races, 478 were caught in stables and only 3 in houses. BARBER and RICE found in Albania and Northern Greece that 50 per cent. of the *elutus* contained human blood, but only 6 per cent. of the *typicus* and *messiae* contained it. Again, they found 42 infected *elutus* for every single infected insect of the other varieties. It is probable that there is a profound cleavage between the barred-egg group (*typicus*, *messiae*, and *melanoon*) and the spotted-egg group (*atroparvus*, *labranchiae* and *elutus*) which favour saline water.

The races *typicus* and *melanoon* are rarely, if ever, associated with malaria.

The race *messiae* is effectively deviated by animals in summer and goes into complete hibernation in winter. It was associated with some outbreaks of benign tertian shortly after the war, and more recently in Rumania.

The race *atroparvus* is not dangerous as a rule, but slight variations in its environment can make it so. It is responsible for whatever malaria occurs in northern Europe. Much depends on the standard of living and the way people house themselves and their animals. The range of *atroparvus* is the whole coastline of northern Europe

from France, through Great Britain, Holland, Sweden, Denmark, Germany to Danzig and beyond; but malaria is endemic only in the coastal area of Holland and a small contiguous zone of German East Friesland. Here the same variety of insect is prevalent all along the coast, and the difference must lie in the environmental circumstances which induce this mosquito to feed on man in one place, and on animals in another. Where *atroparvus* is present, war, indigence or squalor may bring malaria. In Holland, *atroparvus* feeds on animals during the summer, but it does not go into complete hibernation during the winter; though it continues to feed it ceases to lay eggs, and is therefore not obliged to leave its shelter (gonotrophic dissociation). If an infected *atroparvus* shelters in a house it remains "fixed" there, and transmits the infections during the winter which are responsible for the spring epidemic of benign tertian in Holland. On the north coast of Germany, *atroparvus* is found in houses during the summer.

The races *labranchiae* and *elutus* are always associated with an intense malaria, and they try persistently to enter bedrooms even when there is an abundance of animals. They are the mosquitoes of the Mediterranean littoral.

The Geographical Distribution of the several Types.

Maculipennis.—This is the preponderating variety in Norway, and is found in almost pure culture in the Black Forest and Harz Mountains of Germany. It is not found in England.

Messiae.—This variety is probably numerous in all the fresh water regions of Europe. The most southern points of its range are Italy and the Balkans. It is found in Sweden, Denmark, Germany (the lakes of Holstein and Mecklenburg, the valleys of the Oder and Rhine, the Bavarian lakes), France, England, Northern Italy, the valley and delta of the Danube in Rumania.

Melanoon.—This closely related form is found in the rice fields of north Italy and north-eastern Spain.

Atroparvus.—This salt water breeder is found all along the northern coasts of Europe, Warnemünde on the Baltic, the marshes at the mouth of the Elbe, the low marshes of the Netherlands, the mouth of the Thames, Hayling Island. Inland, it is met with on salty soil; for example: near Lübeck, near Bucharest, in the steppes. In some places, it is found breeding in fresh water: in Buckinghamshire, and near Hamburg.

Elutus.—This variety displaces *atroparvus* in the south, and is found along the Montenegrin and Dalmatian coasts, the Balkan Peninsula, Asia Minor, Syria, Palestine, Persia, North Africa.

Labranchiae.—This begins to take the place of *atroparvus* in the north of Italy and is the dominating variety in the Roman Campagna, the Pontine marshes and the west coast of Italy.

Atroparvus, *labranchiae* and *elutus* are the three varieties of *A. maculipennis* which are chiefly concerned with malaria. They lay spotted eggs, and they can breed in saline water. *Atroparvus* is the only race of *maculipennis* found breeding in cool, northern water of moderate salinity. *Labranchiae* prefers the same kind of breeding-place, namely brackish marshes along the coast; but this variety is found in warmer waters, further south. *Elutus* occurs over a wider range than *labranchiae*, but in the same kind of breeding-place. It can breed in waters of higher salinity than *labranchiae*. It breeds in fresh water in Palestine. *W. F.*

i. EKBLOM (Tore). Les races suédoises de l'*Anopheles maculipennis* et leur rôle épidémiologique. [**The Swedish Races of** *A. maculipennis* **and their Rôle in Epidemiology.**]—*Bull. Soc. Path. Exot.* 1935. Apr. 10. Vol. 28. No. 4. pp. 284–289. With 2 figs. (1 map).

ii. SERGENT (Et.). Au sujet des variétés de l'*Anopheles maculipennis* du groupe *labranchiae*. [**The Varieties of** *A. maculipennis* **of the** *labranchiae* **Group.**]—*Ibid.* p. 290. With 1 plate.

i. Although in Sweden malaria is now only sporadic, and the attacks diagnosed as such are generally of foreign origin, indigenous but very rare cases occasionally occur, forming a striking contrast to great epidemics of the past, which at certain times involved a large portion of the country. Thanks to BERGMAN (1877), we possess exact knowledge of the local distribution of the malady in the middle of last century.

Relying on egg-characters, the validity of which has been disputed by ROUBAUD and GASCHEN (see this *Bulletin*, Vol. 30. p. 611), the author finds that, in addition to typical *A. maculipennis*, the races *messeae* and *labranchiae* occur in Sweden as in Italy and Holland. While *messeae* is generally distributed throughout the anopheline area, the other two races are of less regular occurrence, and *labranchiae* appears to be mainly confined to the south coast ; on the west coast it is replaced by *messeae* and *typicus*, and on the east coast by *messeae*. North of the line Kalmar-Kungsbacka the two last-mentioned races alone are found. In the interior the typical race preponderates.

A comparative study of the distribution in Sweden of the three races of *A. maculipennis* mentioned above, and of the bygone occurrence of malaria, both epidemic and endemic, shows that :—

(i) *labranchiae* is absent from most of the quondam malarious regions ;

(ii) *typicus* predominates in those parts of the country where malaria was formerly epidemic as well as endemic ;

(iii) round Stockholm, where in 1927 there were a few sporadic and apparently indigenous cases of malaria, the local races of *A. maculipennis* are *messeae* and *typicus*, which, as vectors, have previously been considered of less importance than *labranchiae*.

It is not absolutely certain that the Swedish races of *A. maculipennis* are identical with, *e.g.*, those found in Holland.

ii. In the vicinity of Algiers, 90 per cent. of female *A. maculipennis* lay eggs of pure *labranchiae* type ; the eggs of the remaining 10 per cent. exhibit characters intermediate between those of the eggs of the latter and those of the eggs of ROUBAUD's recently described var. *sicaulti* (see p. 814 below).

A brief addendum by ROUBAUD admits that the eggs figured by the author as deposited by his " remaining 10 per cent." are very similar to, if not identical with, those of var. *sicaulti*. It would be interesting, by means of a study of selected broods, to determine the race and geographical distribution in Algeria of Anopheles laying indistinctly speckled eggs. *E. E. Austen.*

SERGENT (Et.) & TRENSZ (F.). Premières études sur les races d'*Anopheles maculipennis* en France et en Algérie (1933). [**The Races of** *A. maculipennis* **found in France and in Algeria, in 1933.**]—*Arch. Inst. Pasteur d'Algérie.* 1935. Mar. Vol. 13. No. 1. pp. 1–10. With 6 figs. on 1 plate.

The only race of *A. maculipennis* hitherto met with by the authors in Algeria (three localities) is *labranchiae*, which is indifferently zoophile,

since the adults bite man and domestic animals alike ; and, whether they feed upon human or animal blood, the maxillary index (14 to 15 on the average) is the same. It does not appear that the Algerian *labranchiae* has become less dangerous in the localities studied, where the insects have long found conditions favourable to the development of zoophily.

As regards France, at Moustolat, a village in the Limousin (Corrèze), malaria disappeared more than fifty years ago. The dappled Anopheles eggs found and examined there in the summer of 1933 have smooth and transparent floats like cellophane, whereas those on Algerian eggs are wrinkled and finely striated ; the Moustolat eggs are also narrower than the Algerian, and of a slightly yellowish grey. Instead, therefore, of also belonging to the *labranchiae* race as was at first supposed (see this *Bulletin*, Vol. 30, pp. 611–612), the Moustolat Anopheles are really *atroparvus*, and the local existence of this zoophile race, of which the maxillary index was found to be between 16 and 17, is in accord with the present absence of malaria. Two batches of eggs belonging to *A. maculipennis typicus* were also found.

In Alsace, where anophelism is still intense though the inhabitants are not molested, 206 out of 208 batches of eggs examined were found to belong to the race *messeae*, albeit more or less important variations were noted in the general colour of the egg and in the degree of wrinkling of the floats ; in the great majority of the batches (180 out of 208) the floats were strongly wrinkled. A single batch of eggs was entirely black (= race *melanoon*). *E. E. A.*

GALLIARD (Henri). Contribution à l'étude des races d'*Anopheles maculipennis* en Tunisie. [**The Races of** *Anopheles maculipennis* **in Tunis.**]—*Arch. Inst. Pasteur de Tunis.* 1935. Apr. Vol. 24. No. 2. pp. 343–351. With 3 figs. [15 refs.]

After a preliminary discussion and characterization of the races or varieties of *A. maculipennis* in general, the author proceeds to consider larvae collected by him in certain specified localities in Tunis. All belonged to var. *labranchiae*, as did also some thirty batches of eggs, though one batch of entirely black eggs resembled those of var. *melanoon*. Thus in Tunis, as in Algeria, the predominant and perhaps the only race of *A. maculipennis* is var. *labranchiae*. It is certain, however, that *A. elutus* must exist in the coastal region, and this species may also breed in brackish water in the Sahel.

On the other hand, in North Africa, the absence or recession of malaria in a given region must be explicable otherwise than by the distribution of the different races of *A. maculipennis*. The author, in conjunction with SAUTET, has already demonstrated, in Algeria, the exclusive presence of var. *labranchiae* in two regions, in one of which malaria is disappearing, while in the other it is still extremely severe ; and similar conditions have been found by the same investigators in Corsica, where the distribution of the endemic is very irregular, although the anopheline fauna is everywhere the same. It may perhaps eventually be found that var. *labranchiae* in Corsica and North Africa, although so similar morphologically to the same variety in Continental Europe, possesses biological characters which are entirely different.

E. E. A.

ROUBAUD (E.). Variété nouvelle de l'*Anopheles maculipennis* au Maroc, *A. maculipennis sicaulti* (n. var.). [**A New Variety of** *Anopheles maculipennis* **found in Morocco,** *A. maculipennis sicaulti*, **var. nov.**]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 107–111. With 7 figs. on 2 plates & 1 text fig.

At his insectary in Paris the author received living females from an *A. maculipennis* population, which SICAULT had been studying for several years in the region of Rabat, Morocco. The deposition of batches of eggs by these insects, followed by the rearing of a new generation of adults, furnished morphological and biological data showing that the Moroccan individuals represent yet another new race, allied to *labranchiae* and here described under the name given above.

The egg, which has a dusky hue, is blunter at each end than that of *labranchiae*, and, though becoming progressively darker towards the poles, is without the sharply defined dark caps exhibited by the egg of the race in question ; the markings on the middle region, which appears paler in certain lights, are also much less numerous and less sharply defined. In the larva, the branches of the hair on the second abdominal segment are filiform instead of palmate.

In the adult, the white spot in the fringe at the tip of the wing is generally narrower than in *labranchiae*, and scarcely so large as the interval between the end of the anterior branch of the first alar fork and the third longitudinal vein : all the harpagonal spines in the male hypopygium are sharp.

Biologically the new variety is closely allied to *labranchiae*. It is eurygamous (*i.e.*, will not mate in a confined space) and homodynamous, ovipositing in winter at a medium temperature ; it is also paucidentate, with a maxillary index of about 13·7, and by predilection androphile rather than zoophile. *E. E. Austen.*

RIVERA (Julio) & HILL (Rolla B.). Persistencia de los caracteres diferenciales de los huevos, larvas y adultos, en diferentes generaciones de *Anopheles maculipennis* (*atroparvus*). [**Persistence of Differential Characters in Eggs, Larvae and Adults of Different Generations of** *A. maculipennis*.]—*Medicina Países Cálidos.* Madrid. 1935. July. Vol. 8. No. 7. pp. 313–319. [13 refs.] English summary (7 lines).

Authors' summary :—

" From May to October six generations of *A. maculipennis* var. *atroparvus* were raised, beginning with a single fertilized female. Egg, fourth stage larva, and male and female characters were studied in each generation. Each generation bred true to type for differential characters. Slight variations were noted particularly in size of eggs, and float, wing length, maxillary index and duration of developmental stages, which we attribute to environmental influence."

HILL (Rolla B.), OLAVARRIA (Jose) & RIVERA (Julio). Longitud de vuelo del *A. maculipennis* (*atroparvus*). [**Length of Flight of** *A. maculipennis* (*atroparvus*).]—*Medicina Países Cálidos.* Madrid. 1935. June. Vol. 8. No. 6. pp. 265–268. English summary (5 lines).

" In various experiments with stained *A. maculipennis* var. *atroparvus* to test the length of flight it was found that a certain number will fly from 4 to 5½ kms. in 18 to 36 hours, apparently in search of food. The number found is sufficient to account for the presence of anopheles in the center of a protected zone of 4 kms. radius."

OLAVARRIA (Jose) & HILL (Rolla B.). Algunos datos sobre las preferencias hematicas de los *A. maculipennis*. [**Blood Preferences of** *A. maculipennis*.]—*Medicina Países Cálidos*. Madrid. 1935. Apr. Vol. 8. No. 4. pp. 169–176. [11 refs.] English summary (7 lines).

Summary :—

"The results of 2,500 precipitation tests performed on bloods from freshly engorged *A. maculipennis* var. *atroparvus* caught in houses and in stables [in Caceres, Spain] are given, together with the technique of the reactions.

"Approximately 40 per 100 of those caught in houses and 2 per 100 of stable-caught mosquitoes had human blood. Since less than 7 per 100 of the total anopheles production is caught in houses, it follows that a maximum of 5 per 100 feed on human beings one or more times."

A. G. B.

FACCIOLI (Domenico). Sulle varietà di *Anopheles maculipennis* presenti nella piana di S. Eufemia (Calabria). [**Varieties of** *A. maculipennis* **in the Calabrian Plain.**]—*Riv. di Malariologia*. Sez. I. 1935. Vol. 14. No. 2. pp. 167–184. With 1 fig. English summary (9 lines).

"In Calabria—Piana di S. Eufemia—four varieties of *A. maculipennis* (that is: *labranchiae*, *maculipennis*, *messeae*, *elutus*) are found. The *labranchiae* variety predominates and is the dangerous vector of malaria. All the varieties of *A. maculipennis* are found more frequently associated with animals than with man. The commonest egg type of *labranchiae* is somewhat different from that we observe in other regions. The greatest number of ovipositions is given by the anopheles caught in the stables; the zoophile and anthropophile anopheline races show their highest or lowest percentage of oviposition" in different months of the year.

H. H. S.

KHARITONOV (D. E.). **Observations on the Biology of the Malaria Mosquito** (*Anopheles maculipennis* **Meig.**) **in the Manchazh Subdistrict of the Ural Province.**—*Bull. Inst. Rech. Biol. Perm.* 1934. Vol. 9. No. 6–8. pp. 297–309. [10 refs.] [In Russian.] [Summarized in *Rev. Applied Entom.* Ser. B. 1934. Dec. Vol. 22. Pt. 12. p. 239.]

"A detailed account is given of observations on the adults of *Anopheles maculipennis*, Mg., carried out in the spring and summer of 1925 in the south-west of the Ural Province. In most of this area there were apparently three generations in the year, the adult males occurring in mid-June, mid-July and early August; but in one locality, where streams, etc., dried up by the middle of July, there were only two generations. Females with developed fat-bodies were first observed in the second half of July and became very abundant during August. Of the females found hibernating in April, 90 per cent. were in warm sheds for cattle, pigs and sheep; of the other types of shelters, basements of unheated buildings were preferred, and only a few mosquitos were taken in basements and rooms of inhabited houses. Some occurred in suitable quarters at a distance of nearly a mile from water and at a level of about 100 ft. above the ground. They chiefly congregated on ceilings and the upper parts of walls, especially in corners. They seldom assumed the typical Anopheline resting position, usually resting in the same way as *Culex* does. Badly built animal quarters with large cracks in the walls were avoided. Activity was resumed about mid-April, and active oviposition apparently occurs in the field in the first half of May. In the second half of April, females oviposited in the laboratory within 4½–8½ days after a blood meal, and females taken in hibernation quarters at the end of the month and containing fresh blood did so in about 3 days. The number of eggs laid varied

from 89 to 248. In the summer, most of the mosquitos occurred by day in warm sheds for domestic animals, and only a few in dwellings and outhouses."

HOFFMANN (Carlos C.). La formación de razas en los Anopheles Mexicanos. I. *A. maculipennis* y *A. quadrimaculatus* y una raza nueva del *maculipennis*. [**The Formation of Races in Mexican Anopheles. I.** *A. maculipennis, A. quadrimaculatus* **and a New Race of the Former.**]—*An. d. Inst. Biol.* 1935. Vol. 6. No. 1. pp. 3–22. With 20 figs. [31 refs.] German summary.

A. quadrimaculatus, found in Mexico in a form indistinguishable from that which occurs in Southern U.S.A., is a denizen of the Gulf coast, and does not penetrate far inland. Statements by previous writers, as to its occurrence in the uplands and mountain valleys of the interior, in reality refer not to this species but to a new race or form of *A. maculipennis*, of which, in its various stages, a detailed description is given in this paper under the name *A. maculipennis aztecus*. The egg is described as light brown, without spots ; the floats occupy roughly 40 per cent. of the total length, and have 25 ribs and a finely granular intercostal membrane.

At an altitude of upwards of 7,000 feet (2,250 metres), *A. m. aztecus* occurs throughout the year. During winter, when the males disappear, the females are found in houses ; larvae in all stages are to be met with at any time, and even survive being frozen over for a brief period. Breeding takes place by preference in ditches, containing clean water well supplied with algae and protozoa ; rearing in the laboratory presents no difficulty. *E. E. A.*

EJERCITO (Antonio). **Biological Control of Anopheline Vectors of Malaria in the Philippines : Preliminary Report.**—*Jl. Philippine Islands Med. Assoc.* 1935. Apr. Vol. 15. No. 4. pp. 177–194. With 4 figs.

The experimental damming and flushing of a stream reduced the number of *A. minimus*.

A series of dams provided with gates was constructed in a stream, dividing it into six sections. The stream was flushed at intervals by opening the gates and setting free the imprisoned water. The average number of *A. minimus* (the principal carrier), per dip, taken before the damming of the stream, was 2·45. The average, per dip, after " the stream had been disturbed by flushing now and then," was 0·73 per dip. *A. maculatus*, which is normally an " accidental or seasonal breeder," bred in the dammed up water and was found in the lower parts of the stream after flushing, although there was none there before. Cutting down the shade along the sides of streams is recommended because observations have shown that while *A. minimus* var. *flavirostris* could be found in the shady reaches of the stream, none was present in the portions where the shade had been cleared away. *W. F.*

SINTON (J. A.) & MAJID (Syed Abdul). **The Dispersion of Anopheline Larvae by the Flow of Streams, and the Effect of Larvicides in preventing this.**—*Records of the Malaria Survey of India.* 1935. Mar. Vol. 5. No. 1. pp. 3–17.

Larvae which drifted into a controlled area in the intervals between the applications of Paris green were not destroyed (see AMBIALET, p. 134 above).

A slowly moving stream was treated regularly with Paris green; but in spite of this numerous large anopheline larvae and pupae could be found in it on the next day after each dusting. It was suspected that they had drifted in from the upper reaches. In order to investigate this, a net or barrier made of muslin was stretched across the stream, with about 10 inches of its width above the surface of the water and 10 inches below. The muslin strained off the material floating down the stream, and this was collected and examined. The result showed that in this stream, which flowed at the rate of 300 yards an hour, about a thousand larvae and pupae drifted into the controlled area every hour. Though the Paris green dusted in the controlled area had an excellent immediate effect, it soon drifted away and sank; consequently it had no effect upon the larvae which drifted into the area during the 5 days' interval between the dustings. The continuous application of oil, made by means of oil-balls, greatly diminished the number of larvae which drifted into the controlled area. *W. F.*

TILLI (Pietro). Esperimenti pratici di disanofelizzazione idrica nell'Agro Romano mediante la calciocianamide. [**Practical Experiments with Calcium Cyanamide as a Larvicide.**]—*Riv. di Malariologia.* Sez. I. 1935. Vol. 14. No. 2. pp. 192–200. French summary.

The author's previous tests with calcium cyanamide (nitroline) as a larvicide have been referred to [see this *Bulletin*, Vol. 31, p. 189). In the present article he gives an account of further experimental work in the field using new road-dust as a diluent and in strengths from 10 to 50 per cent. applied every 8, 15, or 20 days. It acts best in a strength of half and half, at which it kills anopheles and culex. It is destructive to the plankton on which the larvae feed. The compound, however, has drawbacks. It causes a high mortality among Gambusia and therefore cannot be employed in waters where fish are preserved; it also arrests vegetation; it sets up conjunctivitis and dermatitis in those working with it unless glasses and gloves are worn and it is well to use long tubes for projecting the mixture.

Although the author mentions the destructive action of the cyanamide on vegetation he recommends its use in rural districts "because it possesses at the same time larvicide and fertilizing properties" and is more economical than Paris green [but the latter is used in a strength of only 1 per cent., whereas the cyanamide needs to be 50 per cent. of the mixture with dust]. *H. H. S.*

DE BENEDETTI (Augusto). Outillage mécanique pour la préparation d'une poussière flottante selon le procédé de Benedetti appliqué par le service de délarvisation de la ville de Milan. [**Benedetti's Apparatus for preparing a Floating Powder.**]—*Rev. d'Hyg. et de Méd. Préventive.* 1935. Apr. Vol. 57. No. 4. pp. 267–273. With 3 figs.

Road dust is no longer obtainable, because the roads are tarred. Ordinary garden soil cannot be used for mixing with Paris green because it sinks at once, but the author has devised a method of mixing it with oil and then heating it, which gets over the difficulty. After the earth has been mixed with the oil, it is heated to 250°C. in one of the portable furnaces used for melting pitch and, after being mixed with Paris green, it is distributed by a blower devised by the author. Figures showing the apparatus are given. *W. F.*

SATYANARAYANA (K.). **Anti-Malarial Operations in the Vizagapatam Harbour Construction Area (1927–1933).**—*Records of the Malaria Survey of India.* 1934. Dec. Vol. 4. No. 4. pp. 343–362. With 2 maps & 5 graphs.

This describes " oil-balls " for using in streams.

Vizagapatam has always been a malarious locality and when the construction of the harbour was begun in 1926 it was feared that there might be a great increase in the disease. The Harbour Authorities consequently decided to take steps to prevent such an occurrence, and they have succeeded not only in maintaining a healthy labour force engaged on the work of construction, but also in preventing an outbreak of malaria in the city while the work was in progress. Some of the control operations were radical and costly. For example, the malarious inhabitants of 4 villages who were a dangerous source of infection to the labour force of the harbour were transplanted to a safer distance, and a tunnel 1,400 feet long was driven through a hill at a cost of 70,000 rupees in order to divert a stream. About 169 wells were filled up, much jungle and prickly pear was cleared away ; streams were canalized and drains were cut, oil and Paris green were used ; a mixture of carbolic acid, kerosene and petrol was used as a spray ; fishing and grazing rights were restricted ; wet cultivation in the neighbourhood of the harbour works was prohibited. " Four Oaks " sprayers were used for most of the oiling, and, in addition, oil balls were employed. These were made by stitching up a mixed mass of waste cotton, Indian corn-cobs and sawdust in gunny bags. They were about the size of a foot-ball and weighed 4 to 5 pounds. They were soaked in oil for 24 hours, during which time they absorbed about 3 pounds. They were then tethered in streams where they made a good film for about a week.

W. F.

JAMES (J. F.). **Fumigation and Trapping of Mosquitoes.**—*Indian Med. Gaz.* 1935. Mar. Vol. 70. No. 3. pp. 143–144. With 1 fig.

The author trapped about 15,000 anopheles in barracks during a period of 11 weeks. Mosquitoes fly towards any lighted exit when a fumigant is burnt. The method adopted was to fix a diaphragm of black cloth over one of the windows of the barracks. In the middle of the black cloth was a hole about 8 inches in diameter. The mouth of a thin muslin bag about 6 feet long was fastened round the edges of this hole, and the blind end of the bag was attached to some object outside the window. All the other windows and the doors were closed, and a coil of a proprietary fumigant burnt. After half an hour the mouth of the bag was tied up, the bag removed, and the contents killed by chloroform. *W. F.*

SERGIEV (P. G.). Sur l'importance épidémiologique de la destruction des moustiques dans l'habitation. [**The Importance of destroying Mosquitoes in Houses.**]—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 4. pp. 315–322. [10 refs.] [In Russian. French summary.] [Summarized in *Rev. Applied Entom.* Ser. B. 1935. Mar. Vol. 23. Pt. 3. p. 76.]

" The author considers that Anophelines in houses should be destroyed in the spring and summer rather than in winter, since most of

them hibernate elsewhere. Moreover, malaria sporozoites are rapidly killed at temperatures near freezing point and do not survive the winter in mosquitos that have become infected in autumn. On resuming activity in the spring, the surviving mosquitos, including those from unknown or remote hibernation quarters, concentrate in inhabited houses, stables and cattle sheds, and should be destroyed from this time onward, but particularly in July, August and September when the rate of infection in them reaches its maximum. In the central part of the northern Caucasus in August 1933 and in Daghestan in August and September 1932, the infection index of mosquitos in houses was as high as 13·5, and 11·36 and 23·58 per cent., respectively."

Ruibinskiĭ (S. V.) & Levit (M. S.). Die Fischzucht als Bekämpfungsmittel der Malaria in der Ukraine. [**Fish-breeding as a Method of controlling Malaria in the Ukraine.**]—*Rev. Microbiol., Epidémiol. et Parasit.* 1934. Vol. 13. No. 2. pp. 151–159. [27 refs.] [In Russian. German summary.] [Summarized in *Rev. Applied Entom.* Ser. B. 1935. Mar. Vol. 23. Pt. 3. p. 86.]

"In the Ukraine, most of the endemic centres of malaria occur in districts with vast expanses of water resulting from river floods. Neglected mill-ponds also offer favourable breeding-places for mosquitos, of which *Anopheles maculipennis*, Mg., is the chief vector of the disease. As it is planned to use large accumulations of water for breeding fish, investigations were carried out in 1932 on the possibility of rendering the fish-ponds unsuitable for mosquito larvae or using the fish against them. For this purpose, over 50 carp-ponds were examined near Kiev. Measures suggested to prevent the breeding of Anophelines include the removal from the water of vegetation, thus depriving the larvae of shelter from the fish, the improvement of the channels by which the ponds are filled or drained and in which Anopheline larvae are often numerous, dusting with Paris green, which, unlike oil, does not affect the fish, and stocking the ponds with young carp, which feed readily on the larvae. The value of other fish in this respect is discussed, and the introduction of *Gambusia* is particularly advocated, as experiments have shown that it can be established in the Ukraine. When a pond is constructed, the bottom should be made very smooth so that it can be thoroughly dried when the pond is drained."

Sicault (G.) & Roule (S.). Note sur la biologie du *Gambusia Hoolbrocki* [sic] au Maroc. [**Biology of** *G. holbrooki* **in Morocco.**]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 134–141.

The multiplication and activities of Gambusia were studied in a swamp 50 by 1 to 4 km. in area connected with two rivers; Anopheles abounded.

An attempt made to drain the swamp by means of a canal proved ineffective and gambusia were introduced. Their fecundity was surprising. In 7 months they stocked an area of 10,000 hectares. Where they were in sufficient concentration in warm weather (at least 20 per sq. metre) they prevented all anopheline increase. In the autumn and even in the spring when the temperature is below 5°C. the fish leave the shallow water for the deeper pools. Larvae can develop at such temperatures; at these times therefore the usual antilarval measures may be employed. *A. G. B.*

BARBOSA (Amando) & ARJONA (Benito López). **El paludismo en el primer año de la vida.**

This book is reviewed on p. 837.

BRITISH MEDICAL JOURNAL. 1935. Mar. 23. p. 590.—**The Malaria Epidemic in Ceylon. First-Hand Experiences.**

In the summary of Dr. V. B. WIGGLESWORTH's lecture on the Malaria Epidemic in Ceylon (p. 732 above), he was reported as having said that to have prevented the breeding of *A. culicifacies* over the affected area would have been a far vaster undertaking than anything so far attempted for the control of malaria. This was misleading: what he really said was, "for the control of *rural* malaria." *W. F.*

CIANCAS RODRIGUEZ (Ramiro). Mi experiencia en el tratamiento del paludismo. —*Medicina Países Cálidos.* Madrid. 1935. Aug. Vol. 8. No. 8. pp. 385–398.

MONNEROT-DUMAINE. Paludisme chez un enfant diabètique. Acidose grave.—*Rev. Méd. et Hyg. Trop.* 1934. Nov.–Dec. Vol. 26. No. 6. pp. 268–271. With 1 chart.

MORIN (Henry G. S.) & CARTON (P.). De l'influence des facteurs climatiques sur la répartition de l'endémie palustre en Indochine.—*Rev. d'Hyg. et de Méd. Préventive.* 1935. Apr. Vol. 57. No. 4. pp. 262–266.

NOVET (D.), BENOIT (G.) & ATMANN (R.). Action thérapeutique de quinoléines à poids moléculaire élevé, homologues de la plasmoquine, sur les hématozoaires des calfats et des serins.—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 729–730. [See this *Bulletin, ante,* p. 117, where, however, the names are spelt differently.]

BLACKWATER FEVER.

PROCEEDINGS OF THE ROYAL SOCIETY OF MEDICINE. 1935. Apr. Vol. 28. No. 6. pp. 671–680 (Sect. Comp. Med. pp. 21–30. [17 refs.] **Discussion on Haemoglobinuria** [BARCROFT (J.), MINETT (F. C.), MACKIE (F. P.), SCORGIE (N. J.), CHRISTOPHERS (Rickard), WEBER (F. Parker), EDWARDS (J. T.)].

Barcroft in opening the debate said that any discussion on haemoglobinuria held in the first decade of this century would, he felt sure, have entailed a discussion of the function of Bowman's capsule and of the rôle played by the glomerular covering. Lately, opinion has crystallized in the direction of the view that Bowman's capsule is simply a filter. Permeability of this filter has been investigated by BAYLISS, KERRIDGE and RUSSELL, who found that of the materials which they tested those with molecular weights of less than 70,000 passed through the membrane and appeared in the urine, whilst those with higher molecular weights were retained in the blood. This is about the molecular weight of haemoglobin, which is consequently just on the border line as regards excretion ; sometimes it will pass through and not at other times.

The question arises whether all haemoglobin molecules are of the same weight, or whether 68,000 is a sort of average weight. The weight which corresponds to one atom of iron is 17,000 ; the complete molecule therefore contains four such units. It might be that all the molecules were uniform and contained four units ; or it might be that the units are loosely attached, in twins, triplets, quadruplets, quintuplets, and so on, but on the average, quadruplets. The matter had been investigated by ADAIR, who decided in favour of the uniformity of the haemoglobin molecules. The molecules of haemoglobin in the red corpuscle appear uniformly to have a molecular weight of 68,000.

Barcroft then passes to the consideration whether haemoglobin found elsewhere than in the corpuscles differs from corpuscular haemoglobin. Within the last year or so the constitution of the pigment in muscle has been investigated, and it appears that myohaemoglobin is not the same as the pigment in blood. Among other differences it has a low molecular weight, and consequently if liberated in the plasma should appear with greater readiness in the urine than does corpuscular haemoglobin. As the spectra of the two forms of haemoglobin are different there should be no difficulty in distinguishing between them in urine, assuming they retain their native properties.

Minett gave a brief summary of the haemoglobinurias and myoglobinurias in animals. He classifies them as follows :—

"*Haemoglobinurias.*

"(1) Due to destruction of erythrocytes by parasites or their products, e.g. certain protozoa, bacterial haemolysins.

"(2) Due to lowered resistance of erythrocytes.

"(3) Of doubtful or unknown origin, e.g. puerperal haemoglobinuria of cows, acute enzootic haemoglobinuria and jaundice in sheep.

"(4) Arising from miscellaneous causes, e.g. certain defined chemical agents, extensive skin burning.

"*Myoglobinurias.*

"Arising from 'destruction' of voluntary muscle : Paralytic myoglobinuria of horses (so-called 'equine haemoglobinuria'). Enzootic myoglo-

binuria of horses (so-called ' equine enzootic haemoglobinuria '). Myoglobinuria of cattle."

Mackie, Scorgie, Christophers and others continued the discussion.

W. Yorke.

STEUDEL (Emil). Schwarzwasserfieber und Chinin. [**Blackwater Fever and Quinine.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. July. Vol. 39. No. 7. pp. 277–287. [11 refs.]

Steudel says that whilst engaged in the production of a new work he had occasion to look through his old monograph entitled " Die perniziöse malaria in Deutsch-Ostafrika " published in 1894, and for the first time he reached a clear conception, chiefly on statistical grounds, of the relationship between blackwater fever and quinine.

Between 1891 and 1893 he treated 18 cases of blackwater, and being firmly convinced that this disease was a form of severe malaria he treated his patients with large doses of quinine, 3 to 5 gm. daily up to a total of 10 gm. The results were excellent ; only three (16·6 per cent.) died, and of these two came to him before he adopted this particular line of treatment, and the third took ill when on a journey and was admitted to hospital only a few hours before death.

In 1895, F. PLEHN drew attention to the fact that blackwater usually followed the administration of quinine, and KOCH in 1897 put forward the theory that blackwater was not due to malaria, because in more than half of the cases malarial parasites could not be found. These observations, and others which followed, caused physicians to withhold quinine in this disease. In a table, Steudel gives the death rate from blackwater in German East Africa during the 10 years 1903–1912. In all 670 patients suffered from the disease and 125 (18·66 per cent.) died. Another table gives the European population and the number of deaths from blackwater during the same 10 years ; in the first 3 years of the period 5·7 per 1,000 per annum of the population died of blackwater, and in the last 3 years 3·0 per 1,000 per annum died of this disease. During the 10 years in question the European population increased four-fold, whilst the number of cases of blackwater increased hardly two-fold. Apparently, therefore, one can conclude that not only the number of deaths decreased, but also that the relative number of cases of the disease decreased very materially. During the 6 years, 1927 to 1932, the English records show that there were 463 cases of blackwater and 118 (25·5 per cent.) deaths.

Steudel asks how it comes that about 40 years ago he had only 16·6 per cent. of deaths, whilst in much later times the death rate appears to have increased. He states that there are two main causes of death in blackwater, viz., anaemia and anuria ; and the latter appears to be the commoner in German East Africa. He adds that it is curious that he never encountered anuria amongst his 18 cases ; in fact he knows of the condition only from reading. He attributes the fact that none of his 18 cases developed anuria to the large doses of quinine which they received. Steudel believes that the quinine prevented the coagulation (Gerinnung) in the renal tubules and thereby prevented suppression of urine, and consequently lowered his death rate.

Quinine, however, increases blood destruction and thus increases the danger of anaemia. If this theory be correct, it is necessary to

seek for new drugs which will prevent the coagulation of haemoglobin in the renal tubules and which will not increase blood destruction.

W. Y.

AMY (A. C.). **Haemoglobinuria on the Indian Frontier. A Second Communication.**—*Jl. Roy. Army Med. Corps.* 1935. Feb. Vol. 64. No. 2. pp. 110–113.

This paper is really a continuation of those published last year and already summarized in this *Bulletin* [*ante*, p. 202]. The author describes another case of haemoglobinuria which ended fatally. This is the first to be reported since August 13, 1933. The patient was an Indian ; the total amount of plasmochin administered was 0·06 gm., spread evenly over 3 days ; the illness was rapid and severe ; and stoppage of the drug immediately after it became evident that something was amiss produced not the slightest effect on the progress of the disease.

The author is still exercising himself on the question whether true blackwater fever occurs amongst natives in the north and north-west of India, or whether these cases are simply and solely due to plasmochin poisoning. He states that, unfortunately, the present case does not help him to solve this problem. *W. Y.*

CHARTERS (A. D.). **A Clinical Study of the Spleen in Blackwater Fever.** —*Jl. Trop. Med. & Hyg.* 1935. Jan. 1. Vol. 38. No. 1. pp. 1–9. [23 refs.]

Clinical notes are given of 15 cases of blackwater fever amongst Indians living in Uganda, and as a result of his observations the author draws certain conclusions regarding the significance of the spleen in blackwater fever.

In 13 of the cases the spleen extended at least two fingers below the costal margin at the beginning of the attack, and it was noticed that a well-marked reduction occurred during the course of the disease. In the author's opinion the severity was proportional both to the degree and the rapidity of contraction of the spleen. Palpable spleens amongst Indian children in Uganda were not found below the age of one, and very large spleens not until after the age of two. Similarly, Indians with less than one year's residence in Uganda did not exhibit palpable spleens, and very large spleens were found only amongst those with over two years' residence.

The author concludes from this that it takes two years for a baby constantly infected with malaria to develop a spleen of over 3 fingers, and approximately the same period for an Indian who has not been in the district before to develop a spleen of similar size. Of 18 Indian patients who developed blackwater fever, 4 had been in Uganda 1 to 2 years, 4 from 2 to 4 years, and 10 for over 4 years. The absence of cases in the first year is to be associated with the rarity of an enlarged spleen.

It has been frequently stated that one attack of blackwater predisposes to another. Charters, however, believes that this is only the case when the first attack has been an incomplete one, *i.e.*, if the spleen has not undergone full contraction. In such cases the first attack is usually a mild one. On the other hand, if the spleen contracts to such an extent as to become impalpable, the patient seems to develop a prolonged immunity. An attack associated with this complete contraction

is usually of a severe nature. Examples are given in support of these contentions.

In dealing with the question of prognosis, Charters lays stress on the degree of rapidity of the contraction of the spleen. If contraction of the spleen is the main factor in the causation of blackwater fever, it is obvious that the greater the degree of contraction the more severe the attack. The study of the author's records shows that the small spleen was, as a rule, associated with a mild attack. Where the spleen is large the prognosis is not so simple. If there is complete contraction from a spleen of over 3 fingers to one that is not palpable, the disease is invariably very severe. For some reason or other it may suddenly stop contracting, and this phenomenon is accompanied by an immediate cessation of haemoglobinuria. The more rapid the contraction of the spleen, the more acute is the course of the disease. A large spleen which undergoes a very rapid contraction may result in a fatal termination before it has disappeared beneath the costal margin; and the very rapid contraction of even a small spleen may suffice to produce a fatal attack of blackwater.

Charters considers that a tender spleen is in an irritable condition and liable at any moment to contract and bring on an attack of blackwater, especially if there is an exciting cause such as a dose of quinine.

As a result of all this, the author believes that the best method of prevention of blackwater, apart from general malarial prophylaxis, is to impress upon the people the importance of regular medical examination, and in any case where the spleen is found enlarged to cause a gradual contraction of the organ by quinine administration. He adds "Should cases prove resistant to quinine, splenectomy will be a certain preventative." *W. Y.*

CASTILLON (L.). Fièvre bilieuse hémoglobinurique, considérations thérapeutiques et pathogéniques. [**Therapeutic and Pathogenic Considerations on Blackwater Fever.**]—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 199–207.

Two cases of blackwater fever were examined with considerable care and a number of observations made on each; these are given in detail. These cases, which ran very similar courses, exhibited certain unfavourable signs, *e.g.*, hepato-renal deficiency, lowering of the cholesteraemia, pronounced anaemia and very poor general condition; favourable signs were:—no diminution in red cell resistance, and passage of more than 500 cc. of urine daily, for "un bilieux qui pisse est un bilieux qui guérit, quelle que soit, par ailleurs, l'importance de son hémoglobinurie." [This seems sound common sense.]

In the author's opinion the cases exhibited certain points of interest from the point of view of therapy and also from that of pathogenesis. To the ordinary methods of treatment the author added subcutaneous injections of chlorhydrate of choline 2 cgm. daily. The blood cholesterin is diminished in malaria and may fall to 0·6 per 1,000. The author states that the action of choline in causing a rise in the cholesteraemia is certain; in his second case it rose to 1·65 per 1,000, which is definitely beyond the normal level.

It is generally recognized that there are two causes which precipitate an attack of blackwater in a malaria subject, viz.:—quinine and exposure to cold. Quinine was no doubt the exciting cause of the paroxysm in the second of these two cases. In the first case, however,

neither of these two factors could explain the relapse of blackwater which occurred when the patient was in hospital under the most careful observation. The author suggests that a simple malarial paroxysm with a rise of temperature to 40°–41·5°C. sufficed in this case to upset the physico-chemical equilibrium of the blood. *W. Y.*

BAMFORD (C. B.). **Observations on Therapeutic Malaria with Special Reference to a Case of Haemoglobinuria.**—*Brit. Med. Jl.* 1934. Oct. 27. pp. 764–765. With 1 chart.

An account is given of a general paralytic, who developed haemoglobinuria following the treatment of his nervous condition by quartan malaria. The strain employed had passed previously through two patients who did not manifest any unusual symptoms. Another patient inoculated simultaneously with the same blood as the case under consideration manifested nothing unusual. When the patient had had ten paroxysms at daily intervals he was put on the usual course of quinine treatment, *i.e.*, 10 grains three times daily, Twenty-four hours later (after he had received 5 doses of quinine) he had a very severe rigor. Quinine was continued, however, and two days later the temperature rose again to 99·6°F. The skin exhibited an icteric tinge and the urine was observed to be unusually dark in colour. The next day the jaundice had deepened and the urine was diminished and of a deep red colour. The serum was found to be of a reddish hue. At this point quinine was stopped and copious drinks were given with large doses of alkalis. The condition responded well to treatment and the urine cleared gradually and became free from albumen within 4 days. *W. Y.*

GOLDBLATT (I.). **Atebrin in the Treatment of Blackwater Fever.**—*South African Med. Jl.* 1935. June 8. Vol. 9. No. 11. pp. 384–385.

This note describes the treatment given to 13 cases of blackwater fever occurring in Europeans during the period 1934 to March, 1935. Of the 13 cases, 3 were very severe—there was thick, black, tarry urine, marked diminution of urine, persistent vomiting and pronounced general toxaemia—2 cases were mild, and the rest were of moderate severity.

The author states that in all his cases the malarial element was very pronounced, and all previous to the attack of blackwater had been using quinine as an anti-malarial remedy. Goldblatt stopped the quinine at once and attacked the malarial parasite with atebrin. All cases were treated in the following way :—

" The patient was given a large dose of magnesium sulphate. Next a diaphoretic powder consisting of aspirin, pyramidon and pulv. ipecacuanha co. āā. gr. v was administered, and the patient placed between blankets. The patient took a hot drink and heat was applied to the kidney areas. Marked sweating proceeded for about 2 hours, when the patient was thoroughly dried, given a dry sleeping-suit, and left to lie between dry blankets, as diaphoresis generally continued mildly for some time. The application of heat to the renal areas was continued. Atebrin in doses of one tablet (0·1 gram) was given at this stage, and a diuretic mixture made up as follows :—

R.

Pot. citrat	gr.xv.
Spt. aether. nit.	m.xxx.
Tr. digitalis	m.ii.ss.
Decoc. scoparii	ad oz.ss.

Sig. : Half an ounce in water every 4 hours.

"The diet consisted of frequent feeds of citrated milk. The patient was encouraged to drink freely of barley-water, diluted orange drink and other bland fluids. Sodium bicarbonate was added to the feeds and drinks and, when the patient could tolerate it, glucose.

"No special treatment was employed for vomiting, but the patient was encouraged to drink freely despite it. Generally it ceased within thirty-six hours."

Under this treatment a marked improvement occurred and within three days the temperature had become normal and the urine clear in all cases. No relapse was observed. The author remarks that it is impossible to state what effect the atebrin had upon the course of the blackwater fever as he had no control cases. *W. Y.*

MURRAY (A. J.). **Blackwater Fever following Atebrin—a Fatal Case.** —*West African Med. Jl.* 1934. Oct. Vol. 8. No. 2. p. 17.

Details are given of a case which supports MOIR's conclusion [this *Bulletin*, Vol. 32, p. 207] that not only are atebrin and plasmochin incapable of preventing blackwater fever, but they may excite an attack.

The patient in question, a European, aged 34, was admitted to hospital at Kaduna, on the 23rd August, 1934, suffering from malaria. He had suffered from blackwater in the spring of 1933, and acting on medical advice he had taken 5 grains of quinine in liquid form daily ever since. On admission the temperature was 103·6°F., the spleen was considerably enlarged, and vomiting was very troublesome. He was given 10 grains quinine on the morning of the day of admission and again in the evening. He had a restless night, and at 7 a.m. the next day he passed porter-coloured urine. Within a few hours the urine cleared and his temperature become normal and remained so until the evening of the 30th August, when it rose to 99·4°. Thereafter it varied between 97°F. in the morning and 99°F. in the evening. On the 28th August the patient was put on 2½ grains of quinine daily, and this was increased to 5 daily on the 6th September. From the 6th September onwards the swing in the temperature was marked, and on the 10th September the quinine was stopped and atebrin, 1½ grains three times a day, commenced. The full course was given, but at the end of it the condition was unchanged. On the 15th September, *i.e.*, the sixth day of atebrin treatment, plasmochin compound was given in addition to the atebrin. The following day atebrin was stopped, and 2½ grains of quinine was given with the plasmochin compound. During the night the patient had a rigor and passed blackwater at 6 a.m. the following day. This did not show the slightest sign of clearing up, and the next day the patient died still passing porter-coloured urine. *W. Y.*

CORMAN. L'association atébrine-extrait de foie dans le traitement de la fièvre bilieuse hémoglobinurique. [**The Association of Atebrin and Liver Extract in the Treatment of Blackwater.**]—*Bull. Méd. du Katanga.* 1934. Vol. 11. Nos. 3 & 4. pp. 77, 79–82; 113, 115–116.

In these two papers details are given of 4 cases of blackwater fever treated, amongst other things, with atebrin and hepatrol. All four patients recovered. *W. Y.*

DÀNG-HANH-KIÊN. La fièvre bilieuse hémoglobinurique et son traitement préventif par la biocholine intraveineuse. [**Blackwater Fever and its Preventative Treatment by Biocholine Intravenously.**] —*Bull. Acad. Méd.* 1935. Feb. 5. 99th Year. 3rd Ser. Vol. 113. No. 5. pp. 191–195.

The article recommends the intravenous injection of biocholine not only for the treatment of blackwater fever, but for certain cases of malaria as a means of preventing blackwater fever.

Blackwater is very common, especially among the Annamites in the upper regions of Tonking. With the old form of treatment (antivenom serum and calcium chloride) the mortality was 30 to 35 per cent. This figure has decreased greatly since the introduction of the biocholine treatment recommended by Dr. RAYMOND. Details are given of a small number of cases which, in the author's opinion, received benefit from the administration of biocholine. Being convinced that the haemolysis in this disease follows a diminution of red cell resistance resulting from hypocholesteraemia, the author decided to add to his quinine an intravenous injection of biocholine as a preventive in all malaria patients who were generally debilitated, or slightly icteric, or who exhibited hepatic or lumbar pain. Since he commenced this line of treatment he has had hardly any cases of blackwater, although in previous years he had from 15 to 24 cases yearly. The amount of biocholine given at an injection—either subcutaneous or intravenous—was 2 centigrams. *W. Y.*

VU-DINH-TUAN. Contribution à l'étude du traitement de la fièvre bilieuse hémoglobinurique par les injections intraveineuses d'urotropine. [**The Treatment of Blackwater by Intravenous Injections of Urotropine.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1934. Dec. Vol. 12. No. 10. pp. 940–954.

Since May, 1932, the author has had occasion to treat 18 cases of blackwater fever at Van Yên on the Black River, Tonking. Certain of these cases have been treated in what the author calls the classical method (serum, biocholine, calomel, calcium chloride, etc.) and others by a new method, viz., intravenous injections of urotropine, and still others by a mixture of the two methods.

The urotropine was given intravenously in doses of 1 gm. morning and evening. The drug was first given to a comatose patient on the fourth day of the disease, and as he got better it was subsequently given to seven other cases at the beginning of the disease. The author says the results were "bien curieux." Within half an hour of the injection the temperature fell by half to two degrees; the urine cleared within 22 hours on an average. The earlier the drug is given the sooner is the disease cut short. The jaundice disappears, and vomiting ceases within 12 to 20 hours and convalescence is greatly shortened.

Clinical details of the 18 cases are given. It is noted that of the 10 cases treated in the classical way (biocholine sera, glucose antivenom, etc.) 30 per cent. died; of the 8 cases treated with urotropine none died. [It is instructive to read this paper in conjunction with that of DÀNG-HANH-KIÊN advocating the use of biocholine. The reader can draw what conclusions he pleases.] *W. Y.*

VAN SLYPE (W.). Thérapeutique calcique dans la fièvre bilieuse hémoglobinurique. [**Calcium in the Therapy of Blackwater Fever.**]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 85–87.

Details are given of two cases of blackwater treated by the author in December, 1932; these patients were treated in the usual way—serum antivenom, rectal glucose, alkalis by the mouth, abundant fluid to drink, atebrin and plasmochin—and in addition they were given calcium gluconate. The first was apparently a case of moderate severity, but the second was more grave and the urine scanty. Both patients recovered and the author believes that the calcium preparation had something to do with this happy result. *W. Y.*

FAIRLEY (N. Hamilton) & BROMFIELD (R. J.). **Laboratory Studies in Malaria and Blackwater Fever. Part III. A New Blood Pigment in Blackwater Fever and Other Biochemical Observations.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Nov. 27. Vol. 28. No. 3. pp. 307–334. With 1 coloured plate & 3 graphs. [29 refs.]

These studies were initiated with the object of getting more accurate biochemical and haematological data regarding what is happening at different stages throughout the course of blackwater fever; the present paper gives further information regarding the new blood pigment which the authors have discovered in blackwater cases [this *Bulletin*, Vol. 32, p. 210], and also the result of their investigation of the bilirubin content of the blood and bile, the blood urea, the alkali reserve, and the blood cholesterol in this disease.

One point which might have been brought out more clearly in the previous paper is the naked eye appearance of the plasma and the various factors responsible for the colour changes. Three pigments were concerned, viz., oxyhaemoglobin, methaemoglobin and bilirubin; if present alone the first imparts a red tint to the plasma, the second a brown, and the third a bright yellow. When there is a mixture of these pigments, as in blackwater fever, their resultant colour depends upon their relative and absolute concentrations. This fact is demonstrated in a coloured plate.

The new blood pigment.—This pigment was constantly present, but in variable amounts, over a period of 10 days in the plasma of Case 7. It resembles methaemoglobin spectroscopically, but differs in not being reduced with Stokes' reagent or ammonium sulphide and in never appearing in the urine in demonstrable quantities. It was never found within the corpuscles and differs from sulphaemoglobin in several important respects. KEILIN, who undertook its investigation, reports as follows:—

"'The samples of serum marked 17/XII/33 and 21/XII/33 contain a peculiar haemoglobin derivative with a normal prosthetic group, but the globin portion of the molecule is undoubtedly modified. The spectrum has the general appearance of methaemoglobin with the bands shifted, however, about 60 Angström units towards the short wave end of the spectrum. Although it does not reduce with Stokes' reagent the compound contains a trivalent iron. It is easily reduced with sodium hyposulphite and gives a typical haemochromogen (globin-protohaemochromogen). Apart from its spectroscopic resemblance to haemoglobin and its trivalent

iron it has no properties of methaemoglobin when tested with alkali, H_2O_2, H_2S, azide, etc.' "

The history of Case 7, which shows several unique features, is given in great detail and the laboratory findings are recorded in two graphs. Unfortunately, there was no opportunity of examining the plasma during the first 3 days of the disease, but two spectroscopic examinations were made on the 4th day and two on the 5th day, and subsequently the plasma was examined daily until the 17th day and on 6 occasions during the following 15 days. The new pigment was always present until the 14th day, when it disappeared and was not observed again; its concentration, expressed in terms of the dilution factor, varied from 1·5 to 6, as is shown in the graph. As this pigment never appeared in the urine, it was either incapable of being secreted by the kidneys at all or, at any rate, the renal threshold was too high for it to be excreted in a concentration detectable spectroscopically.

Oxyhaemoglobin was present either in small quantities or not at all; the maximum concentration observed was 0·28 per cent. Methaemoglobin was never observed in the plasma, and as the incidence of methaemoglobinuria coincided with an acid reaction of the urine and completely disappeared on the 6th day after the urine became neutral, it is highly probable that it was not " true " methaemoglobinuria at all. The method employed, however, required methaemoglobin to be present in a quantity of 0·665 per cent. before it could be detected, and it is possible therefore that it may have been produced in small quantities and rapidly converted into the new brown pigment.

Other biochemical findings recorded in the graph are commented upon under their appropriate sections later in the paper; but one aspect of special interest was the rapid development in a polyuric type of case of renal acidosis associated with a decreased alkali reserve equalling 33·1 cc. CO_2 per 100 cc. plasma and an inorganic phosphorus value of 7·6 mgm. per 100 cc. on the 4th day of the disease. Nitrogen retention was marked and the blood urea reached the high figure of 340 mgm. per 100 cc. 2 days later.

The Bilirubin content of the blood and bile.—Forty-one estimations of the bilirubin content of the plasma were made in the 7 cases, serial observations being undertaken in 6 of them; the findings are shown in a table. In all the cases the bilirubinaemia persisted for some considerable time after demonstrable haemoglobinuria had ceased—a fact which had previously been commented upon by Yorke, Murgatroyd and Owen [this *Bulletin*, Vol. 28, p. 1.]

Barratt and Yorke (1914) [this *Bulletin*, Vol. 5, p. 254], when studying the relation of bile pigment to haemoglobin experimentally in rabbits found that following the intravenous injection of haemoglobin solution there was a distinct and immediate increase, not only in the concentration of bile pigment, but also in the amount excreted. So far as the authors are aware no observations in blackwater fever have been made on the concentration of bile pigment in human bile, either during life with a duodenal tube or at an autopsy. For control purposes estimations on material collected at autopsy were made in which there was no evidence of obstruction to the biliary system. The quantitative indirect reaction showed that bile obtained from the gall bladder in these control cases contained on an average 700 units or 0·35 per cent. of bilirubin. In blackwater Case 3 the bile contained 3,800 units or 1·9 per cent. of bilirubin, and in Case 6, 4,900 units or 2·45 per cent. bilirubin. It is thus seen that the 5- to 7-fold concentration of bilirubin

in the bile of these two cases agrees closely with the experimental findings of BARRATT and YORKE.

Hyperbilirubinaemia was characteristic of all seven cases investigated, the maximal readings in the four non-fatal cases varied from 7 to 26 units, and in the three fatal cases from 20 to 88·5 units (indirect). Two of the three fatal cases showed oliguria, which in one practically amounted to anuria, while the third succumbed to renal acidosis just as water secretion was beginning to fail.

Blood urea.—An increase was observed in all patients, varying from 54 to 79 mgm. per 100 cc. in the three less severe cases, and from 150 to 372 mgm. per 100 cc. in the five severe cases. In the latter group both patients showing polyuria recovered after a prolonged illness, while the others showing a decreased water excretion died. Urea is a powerful diuretic, and the authors believe that its retention and increase in the blood and tissue fluids is probably responsible for the natural tendency to polyuria, which characterizes so many cases of blackwater which recover.

The alkali reserve.—During recent years a few isolated observations have been made to determine the existence or absence of a state of acidosis by estimating the plasma bicarbonate or carbon dioxide combining-power of the plasma in blackwater fever cases. Van Slyke's criteria have been generally followed: he suggested that the normal range varied from 73 to 53 cc. CO_2 per 100 cc., that mild acidosis existed between 53 and 40 cc., moderate acidosis between 40 and 30 cc., and severe acidosis below 30 cc. per 100 cc. of plasma; clinical manifestations were often confined to the last group.

During the present investigation 32 observations on the plasma bicarbonate or CO_2 combining-power of the plasma were made on the 8 cases of blackwater fever. Estimations were always done in duplicate by van Slyke's method, the blood being oxalated and collected under paraffin to prevent chloride shift: a constant decrease in the alkali reserve, varying from 21·8 to 48·0 cc. CO_2 per 100 cc. plasma, was noted in severely ill patients. This lowering of the alkali reserve was associated with urea retention; and in two instances clinical evidence of acidosis developed. Case 9 died of typical uncompensated acidosis with air hunger, and Case 7 developed dyspnoea but recovered with appropriate treatment.

Blood cholesterol.—The average value of 18 estimations of the whole blood cholesterol in 5 very typical cases was 86·5 mgm. per 100 cc., the minimum being 68·0 mgm. and the maximum 109·0 mgm. per 100 cc. There was a persistent hypocholesterolaemia in both fatal and non-fatal cases and the results were not influenced by blood transfusion.

The paper closes with a discussion on the origin and nature of the haemolytic agent in blackwater fever. The authors have shown that methaemoglobin is the predominant pigment present in the plasma in this disease, and that it has an extra-corpuscular origin from oxyhaemoglobin liberated during an intravascular haemolysis of circulating corpuscles. Both the authors, and the reviewer and his colleagues (1930), failed to demonstrate methaemoglobin in the washed corpuscles of blackwater blood containing this pigment, and consequently there is good reason to believe that both methaemoglobin (and the new pigment) have an extra-corpuscular source of origin.

In blackwater there is, therefore, firstly haemolysis of the corpuscle, and secondly conversion of the liberated oxyhaemoglobin into

methaemoglobin, or the allied new pigment. These facts make it highly improbable that we have to deal either with a true haemolysin or a direct drug effect on the corpuscle, A much more attractive hypothesis is that some derangement of metabolism, associated with chronic subtertian malaria, is precipitated by the administration of quinine or plasmoquine and gives rise to a potent haemolytic substance which first lyses the corpuscles and then acts on the liberated oxyhaemoglobin along the lines already discussed. Whether this action is confined to the backwaters of the circulation or whether it occurs in the general circulation is a matter of conjecture. In the authors' opinion the percentage of total blood pigment is sufficient to explain the blood destruction in terms of a lysis occurring in the peripheral circulation, but the inability to demonstrate either *in vivo* or *in vitro* a lytic substance in the serum or plasma derived from blackwater fever cases may be held to favour the visceral site of haemolysis postulated by the reviewer and his colleagues. It must, however, be remembered that the negative results may depend upon the immediate fixation of the haemolytic agent by the corpuscles or on its fluctuating concentration, which would add to the difficulty of its demonstration unless the specimen happened to be collected at exactly the right time.

Yorke, Murgatroyd and Owen (1930) have shown that several haemolytic crises rather than one isolated haemolysis characterizes blood destruction in blackwater fever, and the authors have confirmed this in several of their cases ; but not all cases fall into this category, as in two instances the haemolysis remained unabated until death. Evidently the haemolytic agent may be present in variable quantity in different cases and at different stages of the same case. Apparently, following a haemolysis the haemolytic agent is decreased or entirely used up, and time is necessary for its production and accumulation in a concentration adequate to produce another haemolytic crisis.

Writing on the subject of the disposal of blood pigment, the authors say that it is generally agreed that in any intravascular haemolysis only a very small proportion of the liberated oxyhaemoglobin appears in the urine. Much of the blood pigment is, of course, dealt with by the reticulo-endothelial system ; here the haemoglobin is considered to be converted into an iron-containing moiety, haemosiderin, which is ultimately deposited in the cells of the liver, spleen and kidney, and an iron-free pigment, haemobilirubin, which circulates in the blood and is converted by the polygonal cells of the liver into cholebilirubin with resulting polycholia. In the present series of cases abundant evidence of hyperactivity of this mechanism was found.

[It is impossible in a summary of moderate length to do justice to this valuable paper. It is greatly to be hoped that all who have to deal with cases of blackwater fever will study it carefully in the original. This might have two results—both excellent in the reviewer's opinion : Firstly, it might encourage a few serious students of the disease to attempt to make similar observations for themselves and thus, by collecting reliable data, make a definite contribution to the solution of the mechanism of this most baffling disease ; and, secondly, it might discourage the many who plunge into print for no discoverable reason, except to demonstrate their complete ignorance of the disease and to add to the enormous mass of rubbish which is the chief characteristic of the literature relating to blackwater fever.]

W. Y.

DEUTSCH (Béla). Ueber Hämoglobinkonzentrationsbestimmung im Blute. [**The Estimation of the Haemoglobin Concentrations of Blood.**]—*Biochem. Ztschr.* 1934. Nov. 14. Vol. 274. No. 3/4. pp. 299–304. With 1 fig.

DÉNES (1932) converted the haemoglobin of blood into haemochromogen and estimated the light absorption of the haemochromogen solution. In order to satisfy himself that this procedure is actually suitable for the determination of the haemoglobin concentration of blood, Deutsch has compared the haemoglobin concentration values given by Dénes' method with those given by methods based upon the oxygen capacity of the haemoglobin. The conclusion reached is that the method is satisfactory. [The paper, which is rather technical, should be consulted in the original by those interested.] *W. Y.*

BLACKIE (W. K.). **The Reticulocytes in Blackwater Fever.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. April 17. Vol. 28. No. 6. pp. 571–578. With 1 graph.

Haematological studies made on 4 cases of blackwater fever showed that a vigorous reticulocytosis followed in the wake of the haemolytic phase of the disease.

A brief clinical outline is given of each of the 4 cases, and the observations made on each are given in tabular form. The observations consisted of (1) red cell count, (2) haemoglobin estimations, (3) colour index, (4) size of red cells, and (5) determination of percentages of reticulocytes. In each case a long series of observations was made. The findings suggest that during the stage of active haemolysis the disease exerts an inhibitory influence on erythropoiesis as manifested by the low reticulocyte counts recorded during this period. Moreover, this inhibitory effect is maintained in spite of the severe degree of anoxaemia induced by gross lack of red cells, and in spite of the stimulant action of free haemoglobin or its derivatives. With the cessation of the haemolytic process active erythropoiesis is established and the reticulocyte count rises with extraordinary rapidity. The maximum response in the 4 cases varied from the 6th to the 14th day after the commencement of erythropoietic activity. In the 3 severe cases the maximum figures were, respectively, 50·8, 52·2 and 53·6 per cent., whilst in the less severe cases it was 26·2 per cent. Thus the magnitude of the reticulocyte response is determined to some extent by the degree of anaemia; another factor of importance is, however, the hypertrophic state of the bone marrow. *W. Y.*

KRISHNAN (K. V.); GHOSH (B. M.). **The Reticulo-Endothelial System in Malarial Haemoglobinuria of Monkeys** [KRISHNAN].—*Indian Med. Gaz.* 1935. Apr. Vol. 70. No. 4. pp. 193–197. [13 refs.] **Part II. The Relation of Spleen to Haemoglobinuria** [KRISHNAN & GHOSH].—*Ibid.* pp. 197–200.

i. In the course of previous investigations the impression was gained that the incidence of haemoglobinuria in monkeys infected with *Plasmodium knowlesi* was higher in those animals in which experimental damage or dysfunction of the reticulo-endothelial system was caused. This impression led the authors to investigate the matter further. *P. knowlesi* causes a low grade infection in *Silenus irus* and *S. radiatus*, but an intense and rapidly fatal infection in *S. rhesus*. In the latter species a certain number of animals (60 per cent.) dying of

severe infection developed haemoglobinuria. The authors ask how it is that all rhesus monkeys, which develop a heavy infection, do not exhibit haemoglobinuria ? Is it because of their increased capacity to deal with haemoglobin, and, if so, what is the basis of this increased capacity ?

The observations recorded in this paper were made on a series of 25 *S. rhesus* infected with *P. knowlesi*. The technique used for identifying reticulo-endothelial cells was the supravital staining technique of Napier, Krishnan and Lal (1932). The cells were classified as monocytes and histiocytes according to their capacity to phagocytose neutral red. Total and differential counts were also made. Serial observations were made from the day the animals first showed parasites in their peripheral blood to the day of their death or recovery.

The 25 monkeys are divided into two groups, viz., Group I, consisting of 14 animals which developed a heavy infection and haemoglobinuria ; and Group II, consisting of 11 monkeys not developing haemoglobinuria despite a heavy infection. By the term " heavy infection " is meant a parasite count of 0·2 to 0·5 million per cmm., corresponding to over 50 parasites per microscope field. As monkeys of both groups tended to die if left untreated, quinine was administered by injection to approximately half the number in each group. The results of the observations are summarized in two tables. Table I shows that there is a distinct difference in the counts of the reticulo-endothelial cells in the two groups of monkeys studied. In the pre-haemoglobinuric state of the monkeys in Group I there is a reduction in the number of reticulo-endothelial cells compared to Group II monkeys. In the latter group the mobilization of the reticulo-endothelial cells was marked and haemoglobinuria did not result, although the monkeys showed as heavy an infection as did the monkeys of Group I. Furthermore, it was noticed that the reticulo-endothelial cells in Group I monkeys, just before haemoglobinuria occurred, were functionally less active, the amount of neutral red ingested by them being very much less than that ingested by the reticulo-endothelial cells of Group II monkeys.

The author concludes from this observation that in the pre-haemoglobinuric state there is a depression of function of these cells. Again, it is interesting to note that in Group I monkeys, which developed haemoglobinuria, the maximum intensity of infection was reached in a very much shorter time than in Group II monkeys, which did not develop haemoglobinuria, *i.e.*, 4 days in Group I as compared with 7·5 days in Group II. The general conclusion drawn from these observations is that a damaged reticulo-endothelial system is a prerequisite to malarial haemoglobinuria.

Table 2 shows the fates of the infected monkeys of Groups I and II, which are divided into Subgroups A and B, according to whether they were treated or untreated. The mortality was higher in Group I than in Group II and treatment produced better results in the latter group. The cause of these differences was investigated by a study of the reticulo-endothelial cell response after haemoglobinuria and treatment.

ii. In this work the effect of the removal of the spleen in monkeys infected with *P. knowlesi* was studied. In all, 118 monkeys were used, and of these 56 were splenectomized and 62 served as controls. Approximately, half the number of animals in the splenectomized and non-splenectomized groups were treated with quinine when the infection reached a definite intensity.

The results are summarized in a table, from which it appears that the incidence of haemoglobinuria is significantly higher in the splenectomized than in the non-splenectomized groups. It is also interesting to note that haemoglobinuria occurred in the splenectomized *irus* and *radiatus* monkeys, which normally never exhibit this sign. Treatment with quinine reduced the incidence of haemoglobinuria in all cases, but did not prevent it.

The paper closes with a general discussion of these results and of their bearing on blackwater fever in man. *W. Y.*

BRENNAN (C. H.). A Note on a Case of Haemoglobinuria in a Ukamba Native. —*East African Med. Jl.* 1934. Oct. Vol. 11. No. 7. p. 226.

GIUNTA (Giuseppe). La febbre biliosa emoglobinurica in Somalia ed i suoi rapporti con la malaria.—*Arch. Ital. Sci. Med. Colon.* 1934. Dec. 1. Vol. 15. No. 12. pp. 899–914. [10 refs.] English summary (4 lines).

HANIFAH (Abu). Een geval van zwartwaterkoorts in Midden-Sumatra.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1935. July 8. Vol. 75. No. 14. pp. 1164–1172. [17 refs.]

REVIEWS AND NOTICES.

DEIMER (Johann Heinrich). **Over biotypen van *Anopheles maculipennis* Meigen, in het bijzonder in westelijk Nederland een taxonomisch onderzoek.** [Biotypes of *A. maculipennis* in the Western Netherlands.] [Thesis for Doctorate of Natural Science at Leiden University.]—256 pp. With 1 plate, 11 figs. & 25 graphs. [11 pages of refs.] Amsterdam: N.V. Boekhandel W. Ten Have.

The argument, which is here presented in full, may be summed up as "The Race Problem, Applied to *Anopheles maculipennis*." That problem, fortunately, does not arise in the case of all anopheles, but relates especially to those of extensive and widely differing distribution. Its great importance lies in this, that difference of race and racial habit is invoked to explain the possibility of "Anophelism without Malaria." As is natural, in a doctorate thesis of the University of Leyden, the subject matter deals mainly with the problem in its application to the Netherlands. Malaria is not endemic throughout the Netherlands—any more than it is throughout the greater part of Europe—and may be said to be confined to North Holland, Western Friesland and the country East of Gronigen. The mosquito concerned with its transmission in the Netherlands is the well known *Anopheles maculipennis*. Two races of this mosquito come into question, *atroparvus*, the small winged and *messeae*, the large winged mosquito. Many characters have been investigated which should provide the means and foundation for immediate differentiation of these races. It must be stated here that the author, in the first part of his work, uses the term "race," or as the case may be "variety," provisionally and that definition of "species," "race" and "variety" receives special consideration later in a special chapter.

The differences between the two races are worked through on a morphological and a biological basis. The latter consideration has given rise to the conception of the "zoophile," or misanthrope, and the "androphile" mosquito. These conceptions lead naturally to the institution of antimalaria measures by "zooprophylaxis" through the provision of a sufficiency of the alternative mosquito host, the cow, and "stable diversion" *plus*, of course, treatment of breeding places. Two biological races of *A. maculipennis* may exist, the one positively and the other indifferently zoophile. If that be so, it is the indifferently zoophile mosquito which is dangerous to man. Positively zoophile races are said to have a maxillary index (mean number of teeth on the maxillae) of under 14 and the indifferent race of over 14. The distinction is questionable. It has long been known that malaria is more apparent in districts where the polder water is brackish only and not in those where it is definitely salt. This fact has been expressed more or less quantitatively in the statement that a 0–40 per cent. admixture tends to the production of a zoophile type. In Leyden (no malaria) the water is salt, in Bolsward (high malaria) is brackish.

Other considerations of a bionomic type such as the effect of temperature and humidity on the life of the mosquito are considered critically. "Gonotrophic" characters are also taken into account. Thus, in the Netherlands, *atroparvus* shows "gonotrophic dissociation" that is to say, continuance of blood feeding even with the suspension of ovulation which sets in with hibernation, while *messeae* on the contrary exhibits "gonotrophic concordance," by which is meant simultaneous cessation

of ovulation and blood feeding during the winter months. Experimental work on the subject during these months, but with temperature raised to 26–27°C., showed that the mosquitoes fed richly on blood, but whereas *atroparvus* laid many eggs *messeae* and *typicus* were definitely slow in ovulation. Experiments on interbreeding of races receive special treatment in a special chapter and it has been suggested that in the neighbourhood of Leyden, where a mixed population of mosquitoes exists, the finding of a number of moderately large *atroparvus* mosquitoes might mean crossing between *messeae* and *atroparvus*. It is interesting to have the various described races of *A. maculipennis* separated out as regards their relation to malaria and their biological characters :—Thus *messeae, melanoon, typicus* and *atroparvus* are animal maculipennes. Where they occur, and where there are at the same time sufficient cows and suitable stables, the contact of the mosquito with man is practically broken and " anophelism without malaria " is the result. In the case of *messeae* there is also a " gonotrophic concordance " which prevents the autumnal infection. *Labranchiae* and *elutus*, on the contrary, are human maculipennes and are the promoters of severe endemic malaria.

The bionomic characters of mosquitoes are perhaps the most interesting but the morphological characters also receive in this work very considerable attention. An extensive treatment of these for eggs, larvae, pupae and imagines, by statistical methods, with frequency distributions, their constants and associated errors, is incorporated and is very important in a taxonomic sense.

Chapter II begins with a statement of questions that have to be answered and these show the general trend of the subject matter in subsequent chapters :—

(1) Is the small-wing *Maculipennis* (*atroparvus*) of the malaria districts of the Netherlands identical with that of the malaria-free districts and could crossing between *messeae* and *atroparvus* explain the absence of malaria ? (2) What are the characters of the offspring obtained by crossing *atroparvus* with *messeae* ? (3) Ought *atroparvus* and the other types of *Maculipennis* to be regarded as races, varieties or species and (4) Is *A. maculipennis*, as a morphologically delimited Linnean species, a subjective philosophic abstraction or an objective reality ?

An answer to the last of these questions is to some extent given by the nomenclature proposed by the author for the " races " of *A. maculipennis*. He departs from the Linnean binary system to adopt a ternary nomenclature and subdivides them as :—*A. maculipennis typicus*, Martini, Missiroli and Hackett 1931 ; *A. maculipennis messeae*, Falleroni 1926 ; *A. maculipennis melanoon*, Hackett 1934 ; *A. maculipennis labranchiae*, Falleroni 1926 ; *A. maculipennis atroparvus*, van Thiel 1927 ; *A. maculipennis elutus*, Edwards 1921.

The main points brought out in the author's summary of his own position are :—

1. Whereas *messeae, melanoon* and *typicus* are the so-called " animal maculipennes," *atroparvus*, although primarily a stable mosquito, can in some districts maintain an endemic malaria. *Labranchiae* for Italy and *elutus* for S.E. Europe are " human maculipennes " and responsible for endemic malaria.

2. The fat body in *messeae* is fully mature by September but in *atroparvus* is still small at the end of October. Investigation of the state of the fat body in *atroparvus*, from a malarial district as compared with that in a non-malarial district gave no confirmation of the idea that crossing took place between *messeae* and *atroparvus*. Neither did the experimental

crossing of *atroparvus* with *messeae* : the character of the progeny (claspette spine ; pupal skin spine) showed dominance of *atroparvus*.

3. *Atroparvus* and *messeae* are morphologically very similar. Although constant structural differences appear to exist between them, in eggs, larvae, pupae and imagines, still the " means " of the different characters of the two types came very close to one another, when the conditions of growth (natural or artificial) were the same.

4. Malariologists call the constant types of *A. maculipennis* " races " and accord to each of them the systematic rank of " variety." . . . The definition of a species receives no uniform acceptance. From a strictly morphological point of view *A. maculipennis* is a species and its types varieties, but from the purely physiological standpoint three kinds can be delimited (*a*) *atroparvus*, *labranchiae* and *elutus*, (*b*) *messeae* and *melanoon*, and (*c*) *typicus*. A compromise is suggested in the nomenclature of the types. It is a compromise between the morphological and physiological standpoints and employs a ternary mode of naming.

5. The complex type of *A. maculipennis* is neither an objective reality nor a subjective abstraction but it possesses a real total characterization as also do the biotypes. *W. F. Harvey.*

BARBOSA (Amando) & ARJONA (Benito López). **El paludismo en el primer año de la vida.** [Malaria in the First Year of Life.]—138 pp. With 1 fig. & 8 graphs. [Bibliography.] 1935. Plasencia, Cáceres : Imprenta " La Victoria " Valdegamas número 20. [Ps. 6.]

This is a most interesting study, well documented, carried out by men who have made the most of good opportunities for observation. These observations are expressed clearly and the reasons for the deductions which the authors make are given, the diction is plain and, in short, this small book is eminently readable and instructive and, in the reviewer's opinion, might with advantage be translated into other languages so that the knowledge and advice contained might reach a wider circle.

Malaria in the very young presents certain special characters of which many tropical practitioners, who have learned of the disease among adults and at home, are quite unaware ; this applies not only to diagnosis but also to the adverse effects on nutrition and development and on other diseases.

This book is divided into ten chapters, each of which contains plenty of food for thought. The first discusses the question of malaria as a cause of abortion and premature labour, for it may cause death of the foetus or expulsion of an infant feeble in constitution, and liable to succumb to what would be a mild infection to a healthy child. A few figures are given : Of 152 pregnant women systematically treated with quinine *per os* and 62 by subcutaneous and muscular injection none aborted ; of 57 with severe malaria, untreated, 12·5 per cent. [? 7] aborted and 35·5 [? 20] gave birth prematurely ; 40 of the children were born dead ; of 68 with untreated benign malaria [? mild attack or *P. vivax* infection] 9·7 per cent. aborted, 33 per cent. had premature labour and half the children were born dead ; of chronic relapsing cases treated [number not stated] 1·8 per cent. aborted, 21 births were premature and one-third of the children were born dead ; of similar cases untreated the corresponding figures were 16, 40–47 and 50 or more per cent. There are various hypotheses as to the reason for malaria interrupting gestation ; fever leading to uterine contraction,

anaemia of the mother leading to death of the foetus, toxins initiating contractions, etc.

Chapter II deals with Congenital Malaria. Many authorities are quoted and their views given and there is an admirable short summary in the course of which the authors state: "Congenital malaria undoubtedly exists but the percentage of cases is very small." All three forms of the plasmodium have been seen in the new-born, a large accumulation of them in the placenta appears to favour the condition but is not a *conditio sine qua non.* Next follows a chapter on Immunity. The authors conclude that there is no cross-immunity between the three species, that persons premunized against the strains present in one region have no effective immunity against the strains of another, and that if real immunity exists it must be very exceptional. Further, that any immunity which may have been acquired rapidly disappears when the parasites have been got rid of, that the degree of immunity is greater after spontaneous cure than after cure by drugs; finally, that immunity is acquired more quickly to *P. vivax* than to *P. malariae* and to the latter more than to *P. falciparum.*

As regards Morbidity and Mortality in the young, sex is shown to have no influence; vital statistics are given with respect to sex, age in months, time of year, etc., in Spain as a whole and in Cáceres in particular. In the first and second three months children have about the same morbidity rates, thereafter they increase in successive trimesters. Chapter V on the Clinical Aspects of Malaria in children is highly interesting. Convulsions or vomiting often replace the initial rigor, or there may be marked cyanosis lasting for 10–15 minutes. Some authorities say that the febrile period is short, but in the experience of the authors it was as long as in adults, and at times longer. The benign tertian infection can produce "pernicious attacks" in a child, the temperature curve is often irregular. In 65 per cent., however, it was typically tertian, in 32 per cent. it was quotidian, in 3 per cent. it was continued; occasionally it was irregular; the quartan type was rarely seen in children under 12 months. Splenomegaly was present in about 80 per cent. of cases, it was more marked in *vivax* than *falciparum* infections, but the degree increased with the number of attacks; occasionally it was almost the first sign. Leucopenia was found in about one-third of the cases of uncomplicated malaria in children. Dyspepsia, vomiting and diarrhoea, perhaps choleriform, are common symptoms, and in children with gastro-intestinal disturbance the malaria is more severe; loss of weight may be marked. Labial herpes is not uncommon; urticarial, scarlatiniform and morbilliform rashes are spoken of, but these, the authors believe, are drug rashes (quinine, atebrin, plasmoquine) rather than due to malaria.

Progress depends on (1) the promptness with which the diagnosis is made and treatment undertaken, (2) the nature of infection, (3) whether the attack is primary or a relapse, (4) intercurrent conditions, (5) the type of feeding, whether natural or artificial. As regards the second of these the authors maintain that in Cáceres there is not much difference in virulence between the strains of *P. vivax* and *P. falciparum.* Treatment is detailed in Chapter IX, both of the primary attack and of the relapse. From this, as summing up the authors' opinions, the following extract is translated:—

"Of the several modes of administering quinine in the treatment of malaria: The *tracheal* route is merely a therapeutic curiosity; the *rectal*

is of value only in grave cases in which nausea prevents oral administration; of the *intradermal* we have practically no knowledge; the *subcutaneous* has little to recommend it, for it has no advantages therapeutically and is liable to cause abscess and sloughing; *intraspinal* merely to complicate a treatment which is fairly simple; the *intravenous* route, as MARCHIAFAVA & BIGNAMI maintain should be reserved for exceptional cases of pernicious malaria in which, owing to a state of collapse, there is hope of rapid absorption by the tissues and of immediate action on the parasites in the blood stream in the viscera and in particular the nervous system. In very young children, however, this is far from easy and we are driven to conclude that in them the only possible routes are the oral and the intramuscular."

"Contrary to widespread belief *administration per os will always be the method of choice in the treatment of malaria in infants.* We do not understand the affirmation of FISCHER and others that the best way of treating malaria in infants is by injection, since the many advantages claimed for intramuscular injection—certainty of dosage, greater efficacy, surety of absorption—have yet to be demonstrated." Later they state, "We declare emphatically that quinine and other specific remedies should be given parenterally only when the buccal route is impracticable."

For first attacks of benign tertian they give 20 cgm. of quinine [the salt used is not specified] daily to children under 4 months, 30 cgm. above that age, for eight days to well nourished and for ten days to wasted children. Treatment by atebrin should not exceed 8 days; 5 cgm. daily to those under 6 months, 10 cgm. for those older, given in two doses after food. After the course no antimalaria remedy should be given till a recrudesence occurs, then as before but using whichever (quinine or atebrin) was not used in the first attack. In relapses the rules of the Malaria Commission of the League of Nations, which are quoted, are to be followed as closely as the state of the patient will allow.

In subtertian infections: for the primary attack quinine alone for 7 days, quinine and plasmoquine for another 7, and then quinine alone again for a further like period, the dose being 20–30 cgm. daily of quinine and 0·5 cgm. plasmoquine under 6 months, 1 cgm. to those above 6 months. If there is doubt as to whether the infection is one of benign or malignant tertian the patient should be treated for the latter. Atebrin should not be given to children with digestive and intestinal disturbance and, when atebrin has been used, plasmoquine should not be given till a fortnight has elapsed and then in a small dose 0·0025–0·005 gm. daily for 5 days.

In conclusion, they affirm that quinine can be given to pregnant women in the usual doses without fear; that abortion following administration of quinine is ascribable not to the drug but to the fever, and that quinine is the best prophylactic to ensure a normal pregnancy in women suffering from malaria.

Illustrative cases are not numerous but those given have been carefully chosen; there is a good and full bibliography. *H. H. S.*

PESSÔA (Samuel B.) & MEIRA (João Alves). **A eosinophilia sanguinea.** 165 pp. [Bibliography.] 1935. S. Paulo, Brasil: Sociedade Editora Medica Ltda. Caixa 1.574.

This is a very full monograph on eosinophilia and leaves one wondering whether the subject is of sufficient importance to warrant such a detailed and exhaustive treatment. The work is divided into four

parts, the first being of a general and introductory character on eosinophilia in man. This contains as much as most persons know ; it starts with defining the normal count and the conception of eosinophilia in man and then treats of the conditions under which the excess is found, including various infections, allergic states, organotherapy, X-ray treatment, rickets, gastric and duodenal ulcer, chronic arthritis, endocrine affections and so on. Indeed, it would be almost a shorter list to give the conditions in which this sign is not found. Where it occurs in so many its value in diagnosis diminishes inversely. [The reviewer remembers a teacher of medicine whose favourite question was " What are the causes of enlargement of the spleen ? " and the number increased session by session till the number reached between 50 and 60, by which time of course its value in diagnosis was reduced to vanishing point.]

Part II discusses eosinophilia in parasitism, especially helminthiasis, and Part II experimental eosinophilia. This is valuable because the normal leucocyte counts of 17 species of animals are given, among them those of the horse, cattle, goat, pig, rabbit, guineapig, Brazilian opossum, coati, capibara, cat, dog, rat, macaque, and camondongo, with the number of animals on which the findings are based and the author who carried out the estimations.

Part IV deals with experimental data obtained in rats. It gives the normal leucocyte formula in these animals, the eosinophile increase in those with helminthic infestations, the counts before and after injection of substances believed to produce eosinophilia, *e.g.*, ascaris extract, and lastly the effect of splenectomy. There is an ample bibliography of 206 references. *H. H. S.*

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